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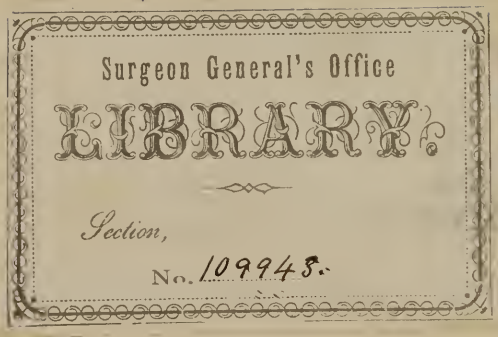

RHEUMATISM

ITS NATURE, ITS PATHOLOGY

AND

ITS SUCCESSFUL TREATMENT

BY

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TO

THE MEMORY OF

ONE OF THE BEST MEN AND MOST ACCOMPLISHED PHYSICIANS

WHOM I EVER KNEW,

MY LOVED AND LAMENTED TEACHER AND FRIEND,

THE LATE DR. J. WARBURTON BEGBIE,

I DEDICATE THIS VOLUME.

PREFACE.

"A PERUSAL of the literature which bears on the question of the treatment of acute rheumatism (rheumatic fever) is a task from which few would rise with any definite idea as to how that disease is best treated. Purgatives, diaphoretics, sedatives, alkalies and alkaline salts, colchicum, aconite, quinine, guaiacum, lemon juice, sulphur, mercury, veratria, tincture of muriate of iron, etc., would each be found to have in turn attracted the favorable notice of one or more of those who have directed attention to the subject. Of all these different remedies not one stands out prominently, as that to which we can with confidence look for good results. We have, indeed, no remedy for acute rheumatism—a malady which not unfrequently proves fatal, which is always accompanied by great pain, and is a fruitful source of heart disease.

"Under these circumstances I need make no apology for bringing under the notice of the profession a remedy which, so far as my observations have gone, has given better results than any which I have hitherto tried—and I have tried all the usual remedies over and over again.

"In the course of an investigation into the causation and pathology of acute febrile ailments, which has for some time engaged my attention, I was led to give some consideration to intermittent and to rheumatic fever. The more I studied these ailments, the more was I struck with the points of analogy which existed between them. On a detailed consideration of these I

shall not now enter. Suffice it to say that they were sufficiently marked to lead me to regard rheumatic fever as being, in its pathology, more closely allied to intermittent fever than to any other disease, an opinion which further reflection and extended experience have served only to strengthen."

Such are the opening sentences of the paper in which, in March, 1876, I introduced salicin to the notice of the profession, as a remedy in acute rheumatism.

In this volume the miasmatic theory of rheumatism, there referred to, is expounded; and an explanation offered of the manner in which the salicyl compounds produce the marked anti-rheumatic effects which they are now all but universally acknowledged to possess.

The plates representing the early changes noted on the surface of the endocardium in cases of rheumatic endocarditis, are taken from Dr. Green's "Introduction to Pathology and Morbid Anatomy." For permission to use them I have to thank Dr. Green and his publisher.

9, Cadogan Place, London, S. W.

CONTENTS.

ON RHEUMATISM.

CHAPTER I.

THE VARIETIES AND SYMPTOMS OF RHEUMATISM.

Rheumatism presents itself in different degrees of severity. It is generally described as occurring in three forms—the acute, the subacute, and the chronic.

For clinical purposes, this is as convenient a classification of its varieties as can be given. It is quite an arbitrary one, however, and is not to be understood as implying more than varying degrees of severity. The three forms have originally the same causation.

Acute Rheumatism, or rheumatic fever, commences with a feeling of cold, occasionally with a distinct rigor, succeeded by unusual heat, a sense of weakness, and general *malaise*. These symptoms are accompanied, or speedily followed, by pains in different parts of the body, especially the limbs. The pains quickly increase in severity and are soon localized in the joints, which become swollen and very tender. The severe initial headache which so frequently ushers in the eruptive fevers, is seldom noted—a diagnostic sign of some importance. Neither is there, as a rule, the same degree of thirst, at least at the commencement. The pain in the limbs is the chief source of complaint.

The inflammation of the joints, which gives rise to the suffering of acute rheumatism, forms the most prominent and characteristic feature of the disease. As a rule, it is confined to the large joints; the knee, ankle, wrist, elbow, shoulder, and hip joints being attacked with a frequency which corresponds very much to the order in which they are enumerated. Of the small joints those of the fingers are most apt to

suffer. In striking contrast with what is observed in gout, the joints of the foot, other than the ankle, are very rarely affected.

The local symptoms of the disease are pain, swelling, and great tenderness, of the inflamed joints. Occasionally there is redness of the surface. But such redness is less marked and less common than in gouty inflammation.

In acute rheumatism the inflammation shows a marked tendency to shift from joint to joint. This alternation of pain, and freedom from pain, may be experienced by all the large joints of the body more than once during one attack of the disease. The invasion of fresh joints is not always accompanied by diminution of the inflammation in those already affected. But occasionally there is noted what seems to be, and is by many regarded as, a true metastasis—a sudden retrocession of the inflammation from one joint to another.

Febrile symptoms are marked. The pulse and respirations are increased in frequency. The temperature varies from 100° to 104° Fahr., but has no distinctive range. The general course of the fever is remittent rather than continued. Just as the local joint affection is made up, not of one long continued attack, but of a succession of short ones, so the febrile symptoms consist, not of one long continuous seizure, but of a series of short ones, whose duration and severity correspond very much to the duration and severity of the local inflammatory attacks. During the whole course of the ailment there is no time at which the patient is free from pain or fever; but there are many ups and downs in the course of both, before the ailment comes finally to an end.

The skin is very active in acute rheumatism. The surface is usually bathed in a profuse perspiration, which is a source of much general discomfort. It has a sour disagreeable odor and an acid reaction. The naturally alkaline saliva is also acid.

The urine is hyperacid, scanty, high-colored, and on standing throws down a copious deposit of urates. Its specific gravity is high, and it contains an increased quantity of urea.

The bowels are constipated. The tongue is coated with a thick white fur. The appetite is gone. There is considerable thirst.

The patient's condition when the disease is fully developed is pitiable in the extreme. He lies on his back unable to move, the least effort to do so causing intense pain. The perspiration trickles down his face,

but he cannot wipe it away. Even the weight of the bed-clothes cannot be borne. He dreads the approach of his friends, screams with agony at the least touch, and sometimes even without such a cause. His expression is that of intense suffering and abject helplessness. He gets no rest. His one desire is to have some relief from pain.

The disease varies in duration; but, when uninfluenced by treatment, the acute symptoms generally last for two or three weeks.

During its course there is a marked tendency to inflammation of the structures of the heart. This constitutes the chief danger and anxiety of the illness; for it is only in exceptional cases that the heart, when once affected, is not permanently damaged; while in not a few the cardiac inflammation proves directly fatal in its acute stage.

The great majority of cases of acute rheumatism do recover. The prognosis, therefore, is favorable.

In some cases, fortunately in very few, the temperature runs up to 106°, 108°, or even 110°. With this high temperature there are associated alarming nervous symptoms. This constitutes that form of the disease to which, from its fatality, the term "malignant" has been applied.

Subacute Rheumatism is a milder form of the same disease, and presents the same symptoms and features in a minor degree.

It comes on more gradually, generally like an ordinary cold, and usually without any initial rigor. Fewer joints are affected at one time; the inflammation of the individual joints is less severe; the pain is less exquisite, and the swelling less marked. There is, however, some swelling, and very decided tenderness. The joint affection shows the same tendency to shift, and vary its seat; but the patient is less helpless, and his general condition less distressing. The perspiration is acid, but not so profuse. The heart is apt to suffer in this, as in the more acute form, but not quite so frequently: when it is affected, the inflammatory action partakes of the generally milder character of the ailment, and is more rarely a source of immediate danger. The remote consequences are apt to be the same in both. The temperature ranges from 99° to 101°. Remissions, and even distinct intermissions, are frequently noted during its course.

Well-marked cases of subacute rheumatism run by insensible gradations into mild cases of the acute form of the disease.

The special features of both forms are so characteristic, and impart to the ailment so distinctive an individuality, that it is not apt to be mistaken for any other disease.

The ailments which most resemble acute rheumatism, are acute gout, acute rheumatoid arthritis, pyæmia, and gonorrhœal rheumatism. As a rule, the differential diagnosis is easy. First, as to acute gout.

Acute gout is a disease of mature years; acute rheumatism a disease of youth. The former generally affects only one joint, the latter several. The former attacks chiefly the small joints, the latter the large. In the former the skin over the affected joint is red and glistening; in the latter, as a rule, redness of the surface is not marked. In acute gout the skin is dry and unperspiring; in acute rheumatism it perspires very freely. In acute gout the blood contains uric acid; in acute rheumatism it does not. Acute gout is not benefited by salicin and salicylic acid; acute rheumatism is speedily cured by them. Acute gout is much less apt to affect the heart.

Acute rheumatoid arthritis resembles subacute rather than acute rheumatism. It is distinguished from it by the following peculiarities Acute rheumatoid arthritis is a comparatively rare disease. It occurs chiefly among young women whose health has already been impaired by some debilitating cause, generally menstrual or uterine disturbance, or prolonged lactation. It comes on more gradually than rheumatism. It attacks the small joints as frequently as the large. It shows no tending to shift from joint to joint. The skin does not perspire as in acute rheumatism, and the secretions are not unusually acid. It is a more obstinate ailment, and does not yield to remedies which speedily cure subacute rheumatism. It does not tend, like this, to affect the heart.

Pyæmia. Cases of pyæmia sometimes occur in which the presence of joint inflammation, possibly also of endocardial inflammation, of febrile symptoms, and of free perspiration, give to the ailment some resemblance to a case of acute rheumatism.

The diagnosis is not difficult. In pyæmia there is the existence of some wound or other lesion to explain its occurrence; the rigors are more marked; the joint inflammation does not shift about, and is characterized by more decided redness of the surface; and the perspiration is not acid. This last feature alone is sufficient to decide the point as to which we have to deal with—pyæmia or acute rheumatism. Should we fail to make a diagnosis by these means, the doubt is not unlikely to be soon set at rest, if the case be one of pyæmia, by the onset of typhoid symptoms, and a speedily fatal result.

Gonorrhœal rheumatism occurs in connection with gonorrhœa. It is not accompanied by the same amount of febrile disturbance as acute or even subacute rheumatism. It affects fewer joints; has a special preference for the knee; and does not show the same tendency to shift about. Acid perspirations do not occur; and it does not tend to affect the heart. Salicin and salicylic acid speedily cure true acute rheumatism. They have no influence on the gonorrhœal form of the disease.[1]

Chronic Rheumatism is a name which is loosely applied to many ailments not really of rheumatic origin. Almost any obscure and obstinate pain, which is not traceable to some other agency, is apt to be attributed to chronic rheumatism. Under this head there thus come to be ranked many aches and ailments which, not being of rheumatic origin, have no claim to the title.

Chronic rheumatism, properly so called, is a milder form of the subacute variety, in which there is not sufficient local inflammation to lay the patient up, or to raise the temperature.

Just as the acute runs into the subacute, so the subacute runs into the chronic by insensible gradations. It is sometimes the precursor, often the sequence, of an acute or subacute attack. It also exists independently of them. "Remarquons d'abord qu'à un dégré très léger, et lorsqu'il n'occupe qu'un petit nombre d'articulations d'un volume peu

[1] The remedies which I have found do most good in gonorrhœal rheumatism, are chlorate of potass and liquor ferri perchloridi, ten grains of the former, and twenty minims of the latter, every three hours.

considérable, le rhumatisme articulaire est souvent apyrétique, à quelque période qu'on examine les malades." [1]

The malady is characterized by the occurrence of pains, obstinate in nature, and sometimes shifting in character, affecting the joints, muscles, and fibrous aponeuroses. When confined to the joints, the pain is frequently symmetrical; that is to say, corresponding joints of opposite sides of the body are apt to suffer alternately or together. The affected parts may be somewhat tender to touch, but are not, as a rule, distinctly swollen. Often only one joint at a time is affected.

The pain is increased by damp and cold. It often disappears in fine, and returns in wet weather.

Unless the patient is in easy circumstances, he may never be confined to the house, and never consult a medical man; but may go about his daily work until he gets better, or until the onset of an acute or subacute attack compels him to lay up.

It is a troublesome ailment which frequently lasts, off and on, for months, and even years. During its continuance there is often laid the foundation of future cardiac troubles. The temperature may now and then rise to 99°, or even a little higher—making the case for the time subacute; but generally it is normal. The pulse is not quickened.

In the age, in the person and family history of the patient, in the shifting character of the pains, and in the occasional slight rise of temperature, we have the best means of distinguishing true chronic rheumatism from the other ailments, gouty, arthritic, and neuralgic, with which it is so often confounded. It is of the utmost importance that such a distinction should be made, for on the accuracy of our diagnosis depends our ability to relieve the patient, and mitigate his sufferings.

There is another morbid condition, which is more properly a sequence of rheumatism than a distinct form of the disease, but which is so apt to be mistaken for the subacute and chronic forms of the malady, that it will be well to refer to it here.

When a man has suffered from repeated rheumatic attacks, there is apt to be induced a state of chronic thickening of the fibrous textures involved in the disease. The nature of the change, and the influence

[1] Bouillaud, "Traité Clinique du Rhumatisme Articulaire."

exercised by it on subsequent rheumatic attacks, will be considered hereafter. Meantime, its existence is indicated with the object of pointing out that this condition, though of rheumatic origin, exists, when developed, independently of the rheumatic poison; and may give rise to symptoms indistinguishable from those caused by it—pain and stiffness of the joints. The importance of recognizing its existence will be apparent when we come to consider the question of treatment.

CHAPTER II.

THE DURATION OF RHEUMATISM.

NEXT to pain and the heart complications, the most notable feature of rheumatism is its prolonged duration.

That the chronic form should be thus characterized, is no more than one would expect in an ailment to which the term chronic is applicable. It is in connection with the acute and subacute forms that this feature calls for special notice.

The long duration of acute rheumatism has been remarked by everyone who has written on the subject.

It is this which imparts to the ailment many of its horrors.

Till very recently it was no uncommon thing for the disease to last for months; and only in exceptional cases did the patient have less than three weeks of suffering.

"In my last attack I was in constant agony for six weeks." "Every attack has laid me up for three or four months." Such are the common experiences of those who are subject to the disease.

There is, however, considerable variety in the duration of different cases. Some are exceptionally long: others exceptionally short. Hence the mean duration of the malady varies with the varying experience of different observers. But all agree in calculating this by weeks rather than by days.

Pinel says that it lasts from seven to sixty days.

Scudamore remarks that "In a case of which the issue is favorable, the fever and pains are brought to a close at the end of the third week; and in slight attacks at an earlier period; but when the course of the disease is untoward, a period of two months scarcely serves to exhaust its power in producing even acute symptoms."

"How long," says Macleod, "a case of acute rheumatism of medium severity might endure, if left to itself, I am unable to say: but, with the common methods of treatment, probably five or six weeks may be about the average duration of rheumatic fever."

According to Chomel, the disease rarely disappears before the twentieth day, and is sometimes prolonged for three months.

Bouillaud states that under the modes of treatment adopted up to the time at which he wrote (1840), the mean duration of acute rheumatism was forty to fifty days: but that under the influence of the treatment to which he had recourse (bleeding *coup sur coup*) it was reduced to less than half that time, *i. e.* about three weeks.

Fuller says that his own observation led him to believe "that even when unattended by any internal affection, the disease, under ordinary methods of treatment, endures from four to five weeks."

Garrod puts it at "from ten days to three or four weeks."

Niemeyer gives the duration of mild cases as "one or two weeks;" and of severe ones as "many weeks."

Senator says that "as a rule acute polyarthritis runs its course in from three to six weeks."

Lebert gives the statistics of 108 cases, of which—

10	lasted	from	.	.	.	.	.	5	to 15	days.
58	"	"	.	.	.	.	.	16	to 35	"
32	"	"	.	.	.	.	.	36	to 55	" and
8	"	"	.	.	.	.	.	56	to 80	"

In Dr. Bristowe's, the most recent English work on Practice of Medicine, published in 1876, the duration of acute rheumatism is thus referred to: "There is no definite limit to the duration of acute rheumatism. Sometimes the patient recovers completely in the course of a day or two, or of a week; more commonly the disease persists for several weeks and not unfrequently it becomes chronic, or is continued by successive relapses for a much longer period than that."

In the St. Thomas' Hospital reports for 1872, Dr. Peacock gives a statistical account of the cases treated in that hospital during the previous year. He there states that the largest proportion of cases recovered in the fourth week. This may be accepted as consistent with general experience.

With regard to hospital statistics on this subject, however, I would remark—and I make the observation on the strength of a large experience of the disease in both hospital and private practice—that severe cases are relatively more frequent in the latter than in the former. Severe

and very acute cases are met with in both; but the proportion of acute to subacute cases is larger in private than in hospital practice.

The only explanation which I can give of this is the difficulty, or even impossibility, of removing a very acute case to hospital during its very acute stage. Over and over again have I seen cases of subacute rheumatism brought into hospital with a history of acute rheumatism of several weeks' duration. The explanation of the delay in sending them generally was, that they were too ill to be moved. And one can quite see the force of that. Very acute cases have their symptoms marked from the commencement. So severe are the articular pains, and so quickly are they developed, that movement is out of the question. A man who cannot bear the weight of the bedclothes, who screams with agony at the least shake of his bed, or at the lightest touch of a friend, is one whom it would be impossible to subject to the jolting and disturbance inseparable from conveyance to another locality. No medical man would recommend such a step; no patient would face the ordeal; and no friends would consent to his doing so.

For this reason I regard hospital statistics as giving to acute rheumatism a rather milder aspect and shorter duration, than would be got from similar statistics taken from private practice. For the same reason I regard Dr. Peacock's statistics as probably under rather than overstating the mean duration of all cases of acute rheumatism.

Such are the statements of the best authorities. All agree in ascribing to acute rheumatism a mean duration of several weeks. And this consists with the experience of every practitioner.

No one who has seen much of the disease (and who that has practised in this country for any time, has not had ample experience of it?), can fail to recall, on the one hand, cases in which the patient, to the delight of himself and attendants, got over the attack in one or two weeks; and, on the other hand, cases which dragged on their weary and painful course for six or eight weeks, and even more. Both courses seem to be equally common under all the old forms of treatment.

The duration of the disease is determined by the duration of pain, its most prominent and characteristic feature. Pain, of course, is only one symptom, but it is that which is most characteristic, which is most complained of, which continues so long as the rheumatic poison exercises

its action on the joints, and without which rheumatism cannot be said to exist in the joints.

The temperature may decline, the pulse may fall, the perspirations may cease; but so long as pain remains in any of the joints, the patient is not convalescent, and may have a re-accession of all his symptoms.

Now-a-days we have in the thermometer a delicate means of determining the duration of the febrile symptoms, which are an essential characteristic of acute rheumatism. It is found that the objective evidence thus got, accords very closely with the subjective evidence derived from the patient's feelings, on which our fathers relied. The temperature falls and rises with the decreased and increased pain and swelling in the joints, but rarely comes permanently to the normal standard till the joint pain disappears.

The cases in which the joint pains persist after the normal temperature has been reached, are those in which the chronic form of the disease follows in the wake of the acute, and in which this sequence of events imparts to the attack an unusually prolonged duration, if we calculate this by the duration of the pain alone.

This grafting of the chronic on to the acute form, explains the long duration of those cases in which acute rheumatism is said to have lasted for several months. Such cases commence as acute rheumatism, gradually pass into subacute, and still more gradually into the chronic form. So insensible are the gradations by which the one form runs into the other that, with the thermometer it is difficult, and without it impossible, to say exactly when acute becomes subacute, and subacute chronic. It is seldom, however, that a case remains acute for more than three weeks. It may be acute for that time, subacute for three or four weeks more; then gradually, and without cessation of pain, pass into the chronic form, and so remain for many weeks—the whole duration of the ailment being several months. It is one attack all through; but it is not *acute* rheumatism during its whole course.

The chronic course of such cases, is sometimes interrupted and varied by subacute exacerbations of longer or shorter duration: serving to show that the chronic form of the disease owns the same causation as the acute and subacute forms which precede and follow it.

These very prolonged cases are exceptional. Generally the febrile symptoms and the pain decline and disappear about the same time.

The authorities and statements which have been quoted, existed and were made before 1876, the year in which the salicyl compounds were recommended for the treatment of acute rheumatism.

When we come to consider the duration of the malady under this treatment, it will be seen how vast are its benefits. For whereas this duration was formerly calculated by weeks, it is now estimated by days. Taking pain as the index of its continuance, it will be found that, when the new treatment is properly applied, the disease lasts as many hours as it formerly did days; or as many days as it formerly did months. For, in many cases, the pain is now more effectually and surely relieved in one day, than it formerly was in one month. The temperature, too, fails to the normal very soon after the pain is abolished.

In my own practice, I have come to regard a case of uncomplicated rheumatic fever, in which the pain is not quite gone, and the temperature at the normal, within forty-eight hours of the time that treatment commences, as an obstinate one. And the cases are few in which the pain is not decidedly relieved within twelve, and abolished within twenty-four hours of such time.

CHAPTER III.

THE SEAT OF RHEUMATISM.

Though some difference of opinion is found among old authors as to the exact seat of rheumatism—Latham, for instance, regarding the lymyphatics, and Carmichael Smyth the muscles, as being specially involved,—the malady is now-a-days generally believed to have its seat in the fibrous and serous tissues.

And there is good reason for this belief. The rheumatic poison is found to exercise its action on, and almost exclusively on, particular organs and textures in which these tissues predominate, and which seem to have no other feature in common. The joints, muscles, and heart, are the parts chiefly involved.

In the case of the joints it is not the osseous, but the fibrous and serous elements—the capsules, ligaments, tendons, and tendinous sheaths, and the synovial membranes, which suffer.

In the case of the muscles, it is less the muscular substance, than the white tendinous material in which it terminates, and the fibrous aponeurosis which invests and gives support to it, that are affected.

So with the heart: the white fibrous structure of the rings and valves, and the serous investing membrane, suffer much more than the muscular substance.

Fibrous or serous tissue appears to be requisite to the action of the rheumatic poison, and to the development of rheumatism.

But all fibrous and serous tissue is not equally apt to suffer. The periosteum is a fibrous membrane, and a most abundant one; but it suffers seldom. The dura mater is so too; but it is rarely the seat of rheumatism.

The liver, spleen, kidney, and uterus, have much fibrous tissue in and around them; but the membranes which it forms do not suffer as do the fibrous textures of the joints and heart.

Then there are many joints which enjoy a comparative immunity from the disease. The small joints of the fingers are not often affected.

The small joints of the toes more rarely still. One seldom meets with rheumatic inflammation of the articulation of the lower jaw, or of the joints of the atlas and axis. And I never saw, or heard of, a case in which the articulations of the ribs were involved. And yet all these joints have ligaments, and fibrous and serous tissues.

The pleura, peritoneum, and arachnoid are serous membranes; but they do not suffer as the pericardium does.

With all these exceptions before us, we cannot, without hesitation, accept the view that rheumatism is essentially a disease of the fibrous and serous tissues. It is only a part of these tissues which shows a special susceptibility to the action of the rheumatic poison. The fibrous lining of the interior of the skull and spinal canal; the fibrous membrane which covers the bones externally; and those which invest and give support to the liver, spleen, kidneys, and uterus, far exceed in quantity the fibrous textures of the large joints and of the heart; and yet, for once that rheumatic inflammation occurs in any one of the former, it occurs many hundred times in the latter.

The serous investing membranes of the brain, of the lungs, and of the abdominal organs, far exceed in extent the corresponding membrane of the heart; but for once that any of them is the seat of rheumatic inflammation, the pericardium suffers a hundred times.

And yet we cannot but allow that this view of the nature and seat of rheumatism has much to commend it; for it *is* almost invariably white fibrous and serous tissues that suffer during its course. *But it is fibrous and serous tissues which have a peculiar and special function.*

In structure all white fibrous tissue is very much alike; but in function it varies much. The chief of its functions are—to support entire organs; to bind together and give support to their constituent parts; and to regulate movement.

That which supports entire organs, is instanced in the fibrous coverings and appendages of the liver, spleen, uterus, etc. That which binds together and gives support to their component textures, is instanced in ordinary connective tissue. That which is engaged in regulating movement, is exemplified in the fibrous textures of the joints.

It is this last form of white fibrous tissue which is specially involved in rheumatism.

The chief function of serous membrane is to facilitate movement.

In some organs, which are provided with a serous investment, the movements are so slight that the membrane has no very active function to perform. The only serous membranes engaged in really active work, are the investing membrane of the heart, and the lining or synovial membranes of the larger joints, which, in function, are to be regarded as serous membranes.

Now, putting these various facts together,—finding that the mass of the fibrous and serous tissues of the body are not subject to rheumatism, but that the disease is limited almost entirely to such fibrous and serous tissues as are habitually engaged in facilitating, regulating, and restraining active movement,—we cannot fail to see that *the seat of rheumatism is not fibro-serous tissue generally, but the fibro-serous tissue of the motor apparatus of the body.*

RHEUMATISM IS ESSENTIALLY A DISEASE OF THE MOTOR APPARATUS.

This motor apparatus consists of two distinct parts, having distinct and separate functions—a *loco-motor* and a *vasculo-motor.*

The function of the former, is to move the solid framework of the body; that of the latter, to set in motion the mass of the liquid blood.

The former consists of the voluntary muscles, their tendons and tendinous sheaths, and the fibrous ligaments and serous membranes of the joints. The latter consists of the muscular and fibrous structures of the heart, with its lining and investing membranes.

But not all the fibrous and serous textures of the motor apparatus show this special susceptibility to the action of the rheumatic poison. In the locomotor apparatus, it is found chiefly in the large joints; in the vasculomotor, it is limited almost entirely to the left side of the heart.

In each apparatus the parts which suffer are those in which the fibrous textures are subject to considerable, and often sudden, strain. Indeed, *the susceptibility to the action of the rheumatic poison in a given portion of fibrous tissue, seems to bear a direct relation to the amount of strain which is apt to be thrown upon it.* It is a clinical fact that the joints which suffer most are those which have most vigorous work to do. It is equally a clinical fact, that the only internal organ which is habitually the seat of rheumatic inflammation, is also the only one whose fibrous textures are habitually subject to strain.

The only serous textures which are habitually the seat of such in-

flammation, the pericardium and synovial membranes of the large joints, are also the only ones whose function it is to facilitate vigorous and free movement.

There are fifteen common seats of rheumatic inflammation—two hips, two knees, two ankles, two shoulders, two elbows, two wrists, two hands, and one heart; and the one functional characteristic common to the fibrous textures of all, is that they are habitually subject to strain. They are the only fibrous textures of the body which are so.

But though the fibro-serous tissues of the motor apparatus are the chief seats of rheumatic inflammation, the disease is not absolutely and entirely confined to them. Occasionally, but only occasionally, it occurs in other fibrous and serous textures; the dura mater, and the pleura for instance.

Muscular tissue, too, may also be sometimes affected.

When we have regard to the intimate connection which obtains between voluntary muscles and their fibrous tendons, and note the manner in which the two textures are blended together, and run into each other, we cannot fail to see that inflammation is very likely to extend from the one to the other; so anatomically inseparable are the two, that such a result is at times inevitable.

But independently of the extension of the inflammatory process directly from tendinous to muscular tissue, there is reason to believe that rheumatic inflammation may originate primarily in muscle. In the case of the heart this unquestionably does occur; and such inflammation of the muscular substance of that organ may prove fatal without any primary lesion of the valves or pericardium. In the case of the voluntary muscles, it is not so easy to distinguish between inflammation of their substance, and inflammation of the fibrous tissue which abounds around, and in them. But from what is known to occur in the heart, it is not unlikely that the substance of the muscles may sometimes be affected in ordinary rheumatic attacks.

Rheumatism, then, we regard as essentially a disease of the motor apparatus.

We have now to consider the nature of this disease, and of the changes which it causes in that apparatus.

CHAPTER IV.

THE NATURE OF RHEUMATISM.

The nature of the change which takes place as the result of the action of the rheumatic poison, has been matter of some difference of opinion. The one point on which all are agreed is that it is inflammatory; and according as the inflammation is acute, subacute, or chronic, so we have to deal with a case of acute, subacute, or chronic rheumatism.

The point on which opinions differ is as to the nature of the inflammation.

Rheumatic inflammation has been regarded by some as differing from ordinary inflammation, not essentially, but only in the peculiarity of its seat. By others it is looked upon as specific in nature, as resulting from the action on the fibrous and serous tissues, of a special poison which does not operate in the production of other than rheumatic inflammation.

The former is the view taken by those who regard the disease as the direct result of exposure to cold and damp; the latter that held by those who look upon it as due to the action of a *materies morbi* circulating in the blood.

That exposure to cold and damp suffices to produce acute rheumatism, is an old view which finds its chief support in the fact that the disease often occurs after such exposure. But so frequent is such exposure in this country, that it would be difficult to point out any disease which might not be attribted to this agency, if we are not careful to distinguish between the *post* and *propter hoc*.

It is common to find patients attributing an attack of typhus or typhoid fever to that cause; but no medical man would endorse such a view, though the sequence of events may be clear enough to the patient.[1]

[1] The rigor which ushered in my own attack of typhus occurred when I

If acute rheumatism owned such a causation, it ought to be most common in the coldest climate, and during the coldest weather. But it is a disease of temperate climates, not of the Arctic regions; and in temperate climates, is not always most common in winter.

It ought, too, if caused by cold, to be most common in children and in old people, who have little power of resisting cold: but the reverse is the fact; for the disease is rare before fifteen or after fifty, and is most common at the age at which the power of resisting cold is greatest. If caused by exposure to cold, the joints which suffer most from such exposure, those of the fingers and toes, should also suffer most from rheumatism: the fact is that they are very rarely involved in the disease. Then again, if this be the cause of the disease, how is it that pericarditis so frequently occurs, and pleuritis and peritonitis so rarely? The pleura and peritoneum are just as much exposed to cold as the pericardium, probably more so. And how, on this view, are we to explain the occurrence of endocarditis, and the almost entire limitation of this to the left side of the heart?

Other peculiarities of the disease there are which it is simply impossible to explain on this view of its etiology. The mere enumeration of these will suffice to show, first, that no external agency, and no amount of exposure, is adequate to their explanation; and second, that rheumatic inflammation is possessed of special features and peculiarities which can be accounted for only on the view that it is specific in nature, due to the action of a special poison circulating in the blood, and, therefore, essentially different from ordinary inflammation.

The special characteristics of acute rheumatic inflammation are as follows:—

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was up to my knees in a river in the Highlands of Scotland, whither I had gone in pursuit of my favorite sport, angling. My friends had no hesitation in attributing my fever to exposure and wet. I knew that the disease was contracted in the typhus wards of the Edinburgh Infirmary, in which I had been acting as clinical clerk till within three days of my initial rigor.

Four years later I suffered from typhoid fever. A week before, I had got wet through. Again my friends ascribed my illness to cold and exposure. I knew that the probable cause of it was to be sought elsewhere. The drains of the hospital of which I was at the time in charge, had got something wrong with them, and were being repaired. The drains of that hospital always contain typhhoid stools ; and that, no doubt, was the source of my illness.

1. The tendency to its occurrence is hereditary—transmitted from father to son.

2. It is specially liable to occur at a particular age—being rare before fifteen or after fifty.

3. It is apt to attack the same individual again and again.

4. It does not confine itself to one joint, but affects several simultaneously or in succession.

5. It attacks also the membranes of the heart.

6. It very rarely terminates in suppuration.

7. It is not much benefited by measures calculated to relieve simple local inflammatory action, but is speedily subdued by proper constitutional treatment.

There is no possibility of explaining these peculiarities by any view which does not recognize the existence and operation of a poison circulating in the blood. No permanently external agency can be regarded as adequate to the explanation of any one of them.

1. The hereditary transmission of the rheumatic tendency necessarily involves the idea of a constitutional, not a local, malady. It means that a certain diathesis, or particular state of the body, predisposing to rheumatism, is handed down from father to son. But such transmission can take place only in connection with constitutional ailments. We talk of a gouty, a rheumatic, a strumous, a cancerous diathesis: but never of a pleuritic, a peritonitic, or a nephritic one.

2. The tendency to attack those of a particular age, is a feature which is noted specially in connection with diseases owning a constitutional origin; and which is manifested in rheumatism, as it is in struma, gout, cancer, etc.

3. The liability to repeated attacks in the same individual, equally points to a constitutional predisposition, rather than to an external and accidental agency.

4. The fact that many joints suffer simultaneously or in succession, points to a generally operating internal and constitutional cause. For it is most improbable that an external and local cause could habitually produce inflammation in so many different parts as suffer during a rheumatic attack.

5. The tendency to heart affection can be explained only on the view that the cause of the inflammation exists in the blood. That cold

and damp might give rise to an endo- or peri-carditis is possible; but that the occurrence of such inflammation in thirty-three per cent. of the cases of acute rheumatism can be due to other than a generally acting constitutional cause, is in the highest degree improbable.

6. The rarity of suppuration, no matter how intense and prolonged the inflammation, indicates that rheumatic is essentially different from ordinary inflammation. "I have often known acute rheumatism of the severest kind have the start of the remedy, full ten days or a fortnight, during which nothing whatever has been done for its relief; and when at length the remedy has been applied, it has been cured as easily and rapidly as I could promise myself that it would have been had I taken it in hand ten days or a fortnight sooner.

"Surely here is something remarkable enough to make us stop and think for a moment. An inflammation of the brain, the liver, or the lungs would not thus wait our pleasure or our neglect, and be as curable ten days or a fortnight hence as it is to-day. For inflammation in these organs does not stand still. It is progressive from stage to stage, and each succeeding stage carries it further and further away from the remedy. But it is the very peculiarity of acute rheumatism that it *does*, in a certain sense, stand still. All its actions and movements are simply as forcible and rapid as possible, yet does it stand still. All its energy is expended upon one stage, and there is no apparent progression beyond it. A fortnight ago there was great heat, and nervous and vascular excitement, and great pain and swelling of the joints; and, to-day, the heat and nervous and vascular excitement and pain and swelling are exactly of the same amount as they were at first. There is no more sign of parts disorganized, or parts destroyed, now than then."[1]

7. Finally, the success of constitutional, and the futility of local treatment, complete the proof that in rheumatism we have to deal with an ailment which owns an internal and constitutional, and not an external and local cause.

The general conclusions to which we are led, are (1) that rheuma-

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[1] "The Collected Works of Dr. P. M. Latham," Vol. I. p. 132. New Sydenham Society.

tism consists in inflammation of the white fibrous and serous tissues of the motor apparatus, and especially of those portions which are subject to active movement and strain; and (2) that this inflammation is specific in nature—the result of the action of a special poison circulating in the blood.

The next question which presents itself for consideration is the very important one of the nature of this poison.

CHAPTER V.

THE NATURE OF THE RHEUMATIC POISON.

Blood poisons may be divided into two classes: (*a*) those which are produced within the system; and (*b*) those which enter it from without.

The rheumatic poison is generally regarded as belonging to the former—as being some product of mal-assimilation, or imperfect tissue metamorphosis.

One of the characteristics of acute rheumatism, is the occurrence of profuse acid perspirations. The urine, too, is hyperacid; and even the naturally alkaline saliva has an acid reaction.

This excessive acidity naturally led to the hypothesis that an acid condition of the blood had something to do with the production of the rheumatic symptoms.

Dr. Prout made the definite suggestion that the *materies morbi* was lactic acid, and that the rheumatic symptoms resulted from the accumulation of this acid in the blood.

This idea, enlarged upon and developed by Todd, Fuller, and others, has been accepted by the profession as affording of the causation of acute rheumatism a more satisfactory explanation than any other hypothesis hitherto advanced.

It possesses, moreover, the advantage of affording a definite foundation for a rational line of treatment.

The lactic acid theory has, for these reasons, been very generally accepted, and endorsed by the profession.

Of late years, however, its accuracy has been called in question, and doubts expressed as to the efficacy of the treatment by alkalies to which it naturally led. The failure of the alkaline treatment has, indeed, more than any other cause, tended to bring discredit on the acid theory.

Lactic acid is a product of tissue metamorphosis. It is an unstable

compound, which readily undergoes change, and is excreted by the lungs and skin as carbonic acid and water.

The presence of an excess of it in the system may be due to increased formation, to defective elimination, or to a combination of these two agencies. The most perfect development of the lactic acid theory is that which recognizes this combination.

Lactic acid is formed during the metamorphic changes which take place in muscle. During exercise it is formed in larger quantity than during quiescence; and when the exercise ceases, there is an excess of this acid in the system.

But the exercise which causes increased formation of lactic acid, is accompanied also by increased action of the lungs and of the skin, the channels by which the acid is eliminated, in the form of carbonic acid and water.

Excessive formation is thus counterbalanced by increased elimination, and no accumulation takes place.

But if, at this time, the action of the skin be checked, the metamorphosis and elimination of the lactic acid are arrested, it accumulates in the system, and the symptoms of acute rheumatism result. The action of the skin is checked by anything which chills the surface of the body.

Such is the most perfect development of the lactic acid theory; and such the manner in which this modern theory is combined with the old view as to the efficacy of a chill in the production of rheumatism. The theory is ingenious and beautiful, and is by no means devoid of foundation. But it must not be accepted without a careful and more detailed consideration of the evidence on which it rests.

First, as to the presence of an excess of lactic acid:

The objection has been urged that this acid has not been demonstrated to exist in excess.

Some observers, no doubt, have failed to detect it; but others have succeeded. All recognize the difficulty of doing so. This is an argument in favor of, rather than against, the view that the excessive acidity is due to excess of lactic acid.

For, first, the existence of an excess of some acid is demonstrated by the acid reaction of the perspiration and saliva, and by the hyper-

acidity of the urine. Second, the difficulty of detecting the special acid to which this is due, indicates that it is one which readily undergoes change, and, therefore, readily escapes detection by the chemist. Third, such an acid we have in lactic acid. Fourth, lactic acid is a normal product of tissue metamorphosis, and may therefore exist in excess. Fifth, lactic acid has been found in the perspiration by some observers.

The presence of an excess of some acid we must admit. The evidence indicates that the special one is lactic acid. The presence of an excess of this acid in acute rheumatism, we, therefore, do not call in question.

But it does not follow that the acid causes the rheumatism.

We have now, therefore, to investigate the evidence on which is founded the belief that such a causal relationship does exist.

So important is this point, that we shall devote to its consideration a special chapter.

CHAPTER VI.

THE LACTIC ACID THEORY OF RHEUMATISM.

The arguments adduced in support of this theory are the following:—

1. Acute rheumatism is accompanied by excess of lactic acid in the system; the disease never occurs without such excess; and such excess is found only in connection with it.

2. The injection of lactic acid into the systems of the lower animals, is followed by inflammatory changes similar to those which occur in acute rheumatism.

3. The administration of lactic acid to man, has been followed by symptoms indistinguishable from those of acute rheumatism.

We shall consider each of these arguments.

1. *Acute rheumatism is accompanied by excess of lactic acid in the system, and such excess is noted only in connection with it.*

That no doubt is true; but it is no proof that the acid causes the rheumatism.

It is quite possible that the morbid action which constitutes the rheumatism may give rise to an excess of the acid; and that this excess and the rheumatic symptoms may both result from the same cause.

In the specific fevers there is an increased formation and elimination of urea, another product of tissue metamorphosis; but we do not regard the excess of urea as the cause of the disease. It is merely one of its phenomena. It may indeed, and at times does, give rise to special symptoms, but these form no essential part of the malady.

May it not be with lactic acid in rheumatic fever, as it is with urea in the specific fevers? May not the presence in excess of this product of tissue metamorphosis, be simply one of the phenomena of the disease, one of the results of a morbid process set agoing by another and totally different agency? The excess of lactic acid may, and does, give rise to some of the phenomena of acute rheumatism; but it may do this without being the cause of the disease.

The main, indeed the only, support of the argument which we are considering, is the fact which constitutes it, viz., that there is always an excess of lactic acid in acute rheumatism, and that such excess is found in connection with no other disease.

But there are cogent reasons for not accepting the view that the acid causes the rheumatism.

If it were so, the rheumatic symptoms should persist so long as the acid existed in adequate excess in the system, and should decline when it ceased to do so, and not till then. Remedies, too, which neutralize the acid should also cure the rheumatism; while those which did not do so, should fail to have any curative effect.

But so far from this being the case, we find the contrary prevail.

The early advocates of the lactic acid theory believed that the administration of alkalies, by neutralizing the acid, would cure the rheumatism. And theoretically such should have been the case. But the reality has been very different. For though, in want of any better mode of treatment, alkalies have continued to be, till very recently, the chief remedies administered in rheumatism, we very well know that they exercise little or no control over the disease. They may be given so as to saturate the system, and render the urine alkaline, without doing good to the rheumatism. The disease seems to last as long, and to run the same course when treated by alkalies, as it does when it receives no treatment at all. If the acid caused the rheumatism this should not be.

Again, we find that salicin and salicylic acid cure acute rheumatism effectually and speedily—as will be evidenced further on. It is impossible that their curative effect can be due to any neutralizing action on lactic acid. Their effect is produced also independently of any action on the eliminating organs.

It is certain that these remedies neither neutralize, nor get rid of the acid; for in cases of acute rheumatism which are thus cured, the perspiration and the saliva often continue to give an acid reaction for four, six, or more days after all symptoms of rheumatism, except this acidity, have disappeared.

This continued acidity of the perspiration and saliva, so long after the rheumatic symptoms have ceased, is no doubt due to the presence and excretion of acids formed during the continuance of the disease.

It has an important bearing on its pathology.

It indicates, first, that the acid in the system is neither neutralized nor destroyed by the remedy which neutralizes the action of the rheumatic poison, and puts an end to the disease.

Second, it shows that the mere presence of lactic acid in the system does not necessarily give rise to rheumatic symptoms.

Third, it indicates that it is the *production* of the acid in excess, not its mere *presence* in excess, which is essentially associated with these symptoms. In other words, these symptoms and the presence of an excess of lactic acid in the system would seem to be associated together merely as conjoint results of one and the same action.

Thus the view is forced upon us that lactic acid is not the cause of acute rheumatism, but merely one of the results of a morbid process set agoing by some other agency.

Into the nature of this agency we shall inquire by-and-by. Meantime, we have to consider the other arguments which have been adduced in support of the lactic acid theory.

2. *The injection of lactic acid into the systems of the lower animals, is followed by inflammatory changes similar to those which occur in acute rheumatism.*

Upwards of twenty years ago Dr. Richardson published an account of some experiments made on cats and dogs by injecting lactic acid into their peritoneal cavities.

The result of these experiments has been regarded as favorable to the lactic acid theory of rheumatism; and they are referred to in many English works on the practice of medicine as one of the reasons for accepting that theory.

A careful perusal of Dr. Richardson's paper would seem to indicate that there has been accorded to his experiments a wider scope and greater significance than is their due. For in none of the animals experimented on, was there induced a morbid condition which we would call rheumatism in man. What Dr. Richardson found was, that in animals into whose systems lactic acid had been injected, there was observed, after death, evidence of inflammation of the endocardium.

Endocarditis, and not rheumatism, was the malady induced.

But as endocarditis is frequent, and an excess of lactic acid invariable, in acute rheumatism, the inference was drawn that these experiments demonstrated the accuracy of the view that lactic acid is the morbid agency which gives rise, not only to endocarditis, but also to the rheumatism with which endocarditis is usually associated.

The inference is wider than the facts warrant.

A careful examination of these facts, indicates important points of difference between the induced endocarditis of Dr. Richardson, and that which occurs in connection with acute rheumatism—so important, that we are led to regard the results of his experiments as negative, so far as the pathology of acute rheumatism is concerned; and the inferences drawn from them as quite inadmissible.

The chief difference to be noted is, that in rheumatic endocarditis it is extremely rare for the right side to be affected: while in Dr. Richardson's experiments it was always the right side which suffered. But Dr. Richardson shall state his own case:—

"In the course of my description of the symptoms and morbid anatomy in the case of endocarditis induced by experiment, I dwelt specially on the circumstance that in these instances the disease was primarily manifested on the right side of the heart. At first sight this occurrence is an anomaly when compared with ordinary endocarditis, and hastily glanced at, would serve to break the idea of relationship between induced and spontaneous endocardial inflammation. But a little reflection dispels these hasty inferences, and offers not merely a proof of relationship, but an explanation absolutely of the known fact that in spontaneous endocarditis the left side of the heart is the common seat of the disorder.

"The cause of the difference in the two classes of cases, I mean the induced and the spontaneous, seems then to be simply this: In the cases of induced endocarditis, the poison introduced into the body by an absorbing surface finds its way into the circulation by the venous blood. It follows, that as the poison traverses the circulatory canals, it comes in contact with the inner surface of the right side of the heart first: in the pulmonic circuit it undergoes some loss, and so entering the left cavity is less active in its effects. In other words, the poison in these instances, so far as the heart is concerned, is derived from the systemic circuit, and is lost in part in the pulmonic circuit.

"On the other hand, in rheumatic endocarditis the evidence all points to the supposition that the poison is a product of respiration. Hence, as the poison traverses the circulatory canals, it comes in contact first with the inner surface of the left side of the heart: while in the systemic circuit it undergoes loss or combination, so that the blood returning by the veins is not poisoned, and the right side of the heart escapes.

"Reversing the previous proposition, the poison in these cases, in so far as the heart is concerned, has a pulmonic origin and a systemic destruction.

"The further inference from this argument also is, that the action of the producing poison, both in the artificial and the spontaneous endocarditis, is directly on the part affected, *i.e.*, by contact with the endocardial surface. Let us examine this question from another point of view.

"Seeing that a certain series of changes are produced in the endocardial membrane when the necessary conditions, viz., a producing poison, is present, our reason admits of but two modes by which the changes induced could originate. Either the poison has been carried into the affected part through the nutritive vessel or vessels of the part, and thus has produced its effect *a tergo* by interference with nutrition; or it has been applied to the free surface of the part, and has produced its effect by direct contact, like a blister applied to the skin. Many poisons have the privilege of producing their effects by both methods; but in reference to lactic acid and endocarditis, there is no alternative but to accept that the action of the poison is by direct contact with the free surface.

"For the position of the question is this: that in the artificial endocarditis the right side of the heart is first affected; in the rheumatic endocarditis the left side is primarily, and by a general rule which has but rare exceptions, singly affected. Now it is clear that if the effect of the poison in these cases, one or other, were *a tergo, i.e.*, by introduction to the endocardial surface through the nutritive vessel, the two sides of the heart would share equally in the catastrophe, inasmuch as they are both fed from a common source and the same blood. But if the action of the poison is by direct contact of the poison with the free surface of the membrane, the occurrence of endocarditis in the induced

cases on the right side, and in the spontaneous cases on the left side, is easily and satisfactorily accounted for."

What Dr. Richardson teaches is, that in both induced and rheumatic endocarditis the cause of the inflammation is lactic acid in the blood; and that the acid produces its effect by a direct irritant action on the free surface of the endocardium.

The bearing of his experiments on our subject may be considered under the following propositions, taken from Dr. Richardson's paper, and given in his own words:—

1. "In rheumatic endocarditis the poison is produced in the pulmonary and destroyed in the systemic circulation.".

2. "Lactic acid could not exist in the blood without producing endocardial mischief."

3. "The action of the poison which produces the disease (rheumatic endocarditis) is directly on the free surface of the endocardial membrane: the poison acts, in a word, after the manner of a local irritant."

(*a*) The first proposition is a most important one—so important that it cannot be accepted without evidence; for on its accuracy depends the validity of Dr. Richardson's whole argument.

If some show of reason cannot be given for the belief that lactic acid is produced in the pulmonary, and destroyed in the systemic circulation, then Dr. Richardson's statement to that effect can be regarded only as a hypothesis brought forward to support his position.

If, on the other hand, evidence can be adduced to show that lactic acid, so far from being destroyed, is actually produced in the systemic circulation, then Dr. Richardson's proposition is proved to be erroneous, his position untenable, and his whole argument fallacious. A careful study of the question would indicate that such evidence does exist.

During the process of digestion, sugar is formed. From the digestive organs it passes into the circulation. Part of it is taken up by the liver, and converted in that organ into glycogen, in which form it is stored up in the liver. During fasting it again becomes transformed into sugar, and as such passes into the circulation. Like all non-nitrogenous substances, sugar is finally transformed into carbonic acid and water. In the course of this transformation there are produced various intermediate substances. One of these is lactic acid. The

question which we have to consider is, "Where does this formation of lactic acid take place?" Our knowledge on this point has been so admirably summed up by Dr. Lauder Brunton, that I cannot do better than quote his statement:

"The healthy organism is able to consume not only all the sugar produced within itself, but even more; and if a solution of glucose or glycogen be injected in small quantities under the skin, or even into the veins of an animal, no sugar will appear in the urine. This destruction of sugar probably goes on chiefly in the blood, lungs, and muscles, though it may take place in other tissues as well. Its occurrence in blood after it has been drawn is shown by the sugar contained in it disappearing after a short time when it is kept at a moderate temperature; and there is no reason to suppose that this does not go on within the body, more especially as Binz and Zuntz have shown that the formation of acid, which goes hand in hand with the destruction of sugar, occurs even more quickly while the blood is still fluid, or, as we may say, alive, than after coagulation has taken place. The important part played by the lungs in the destructive process is evident from the great diminution which the sugar sometimes undergoes during its passage from the right side of the heart to the carotid artery; and the powers of muscle in this respect are shown by the observation of Ludwig and Genersich, as well as of Bernard, that the blood which passes through the vessels of a contracting muscle contains much less sugar when it issues from the vein than when it enters the artery. And yet, strangely enough, Ludwig and Scheremetjewski found that after grape-sugar had been injected into the veins of an animal, little or no increase took place in the oxygen consumed, or the carbonic acid given off from the lungs—a result which indicates that grape-sugar, *as such*, is not burnt off in the body. On the other hand, they found that when lactic acid as well as other organic acids, combined with soda, were injected into the veins, the amount both of oxygen and carbonic acid rose greatly, showing that these acids underwent combustion with great facility. Glycerine also undergoes combustion readily. Now, Bernard found that as the sugar disappears from blood, its place is taken by lactic acid: and, as Du Bois-Reymond has shown, an accumulation of sarcolactic acid in muscles occurs after they have been kept in action."[1]

[1] British Medical Journal, vol. i., 1874.

It is evident from this that lactic acid is formed in the blood and in muscle; and, therefore, in the systemic circulation. "Lactic acid is chiefly produced in the muscles by the decomposition of glucose formed from glycogen, a substance produced in the liver."[1]

Dr. Richardson's statement that the acid is formed in the pulmonary and destroyed in the systemic circulation, is thus in direct opposition to the evidence. Indeed, on the view that it is formed in increased quantity during muscular exercise, is based the most perfect development of the lactic acid theory of rheumatism—the theory which Dr. Richardson advocates.

Whether or not we accept Dr. Richarson's view of the mode of production of rheumatic endocarditis, must depend on whether or not we accept as accurate his statement that lactic acid is formed in the pulmonic, and destroyed in the systemic circuit. We find this statement to be in direct opposition to what is known regarding the formation of that acid; we, therefore, reject it, and in doing so necessarily reject with it all that Dr. Richardson teaches regarding the mode of production of rheumatic endocarditis.

(*b*) The second proposition, that lactic acid could not exist in the blood without producing endocarditis, is in direct opposition to facts and experience.

"It is absurd," says Dr. Richardson, "to assume that ounces of an acid of the producing series thrown off from the skin of a sick man should not be derived from his blood." Lactic acid is thus thrown off from the skin in acute rheumatism. If Dr. Richardson's proposition were correct, endocarditis should be an invariable complication of that disease. But it occurs only in a minority of cases. Lactic acid, therefore, frequently exists in excess in the blood, without producing endocardial mischief.

(*c*) The third proposition, that lactic acid acts as a local irritant to the endocardium, is in keeping with the second; but is equally inconsistent with evidence, and is refuted by the same arguments. If lactic acid be the rheumatic poison, and if it exercise a direct irritant action

[1] Outlines of Physiology, by John Gray McKendrick, M.D., F.R.S.E., Professor of Physiology in the University of Glasgow. 1878.

on the endocardium, that membrane should give evidence of irritation in every case of acute rheumatism: it does so only in a minority.

Rheumatic endocarditis ought not to, and cannot rightly, be considered apart from the joint inflammation in connection with which it occurs. The poison which gives rise to the one, gives rise to the other; and its mode of action in the production of inflammation of the fibrous and serous tissues of the joints and of the heart, is doubtless the same. It is physically impossible for lactic acid to act on the fibrous elements of the joints, as Dr. Richardson believes that it acts on the endocardium.

Again, pericarditis is almost as frequent in acute rheumatism as endocarditis. The two are doubtless due to the same cause, and produced in the same way; but Dr. Richardson leaves pericarditis out of account altogether, and gives of the occurrence of inflammation of the membrane which lines the interior of the heart an explanation which cannot apply to inflammation of that which invests it externally.

For these various reasons, we regard the inferences which have been drawn from Dr. Richardson's experiments as fallacious and unwarranted; and the experiments themselves as affording no valid support to the lactic acid theory of rheumatism.

The results of experiments made on the lower animals may readily have their importance exaggerated; and we cannot exercise too great caution in drawing from them inferences applicable to man. Though certain effects are got from the administration of this or that drug to a cat or dog, it by no means follows that like results would follow its administration to man. This objection is peculiarly applicable to Dr. Richardson's experiments. There are abundant observations to show that the only invariable result of the administration of lactic acid to man is increased action of the skin. But this is a result which could not be got in dogs, the animals on which Dr. Richardson experimented, for they do not perspire. So that we could not expect observations made on them to be of value in elucidating the action of lactic acid on man. Dogs and man are so differently constituted that it is impossible that lactic acid could have the same effects on both. This fact greatly diminishes the value to be attached to Dr. Richardson's observations.

But not only may the value of Dr. Richardson's experiments, and the validity of his inferences, be called in question. The accuracy of

his observations has also had grave doubts thrown upon it. For, though they were apparently confirmed by Rioller and Rauch, it was subsequently found by Reyher, in the course of an investigation undertaken at the suggestion of Virchow, that endocardial signs, such as Richardson attributed to the action of lactic acid, were frequently observed in dogs, without any previous injection of that substance. It is, therefore, probable that the signs which Richardson attributed to the action of lactic acid on the endocardium, existed independently of it,—that, in short, the acid had nothing to do with their production, and exercised no action whatever on the endocardium.

3. *The administration of lactic acid to man has been followed by symptoms of acute rheumatism.*

Since Cantani recommended lactic acid as a remedy in diabetes, numerous cases of that disease have been thus treated. In several, the administration of the acid has been followed by symptoms indistinguishable from those of rheumatism, pain and swelling of joints, with rise of temperature.

One of the most remarkable is a case related by Dr. B. Foster,[1] in which there occurred six well-marked arthritic attacks. "The phenomena corresponded in all respects to those which are characteristic of acute articular rheumatism. They came on when the acid was taken, and ceased when it was discontinued. When moderate quantities of the acid were tolerated, an increase in the dose was succeeded by the painful inflammation of the joints. Coinciding with the development of the articular affection was the appearance of perspiration, at first only slight, but afterwards, in the more severe attacks, copious and acid.

"These facts," continues Dr. Foster, "have dispelled the last lingering doubt in my mind as to the truth of the lactic acid theory of rheumatism."

One cannot read the details of Dr. Foster's cases without feeling that we have in their facts strong evidence in support of the lactic acid theory—to my mind, the strongest that has been adduced in its favor. Such evidence cannot be disregarded or ignored: either we must ex

[1] Clinical Medicine, by Dr. B. Foster. 1874.

plain it, or our refutation of the lactic acid theory must remain imperfect and inadequate.

Can it be explained? I think it can; and that even Dr. Foster may be shaken in his renewed allegiance to his old love.

Lactic acid is a product of retrograde tissue metamorphosis. As such, it is a normal ingredient of the system.

Such products have two distinct actions: first, their normal stimulant action on the organ whose function it is to eliminate them; second, their abnormal action on the system when, for any reason, they are retained in the circulation in undue quantity.

The special question of the mode of action of lactic acid as a disturbing agent, must be considered in connection with the wider question of the mode of action of excretory compounds generally.

The excretory compounds with whose action we are most familiar, are carbonic acid and urea. We shall illustrate the probable mode of action of lactic acid, by what is observed in their cases.

Carbonic acid is formed all over the body, and is eliminated by the lungs. It is produced during tissue respiration; it is eliminated during the pulmonary. The immediate and first effect of the presence of an undue quantity of it in the blood, is increased force and frequency of respiration, consequent on its disturbing action on the respiratory centres.

But it has also a toxic action; and when, from any interference with the process of respiration, the acid is not eliminated, death speedily ensues.

The same result is got when, without any mechanical interference with the respiratory act, an animal is placed in an atmosphere of carbonic acid. The mode of death is the same in both cases; for, in the latter, the fatal result is due, not to inhalation of the carbonic acid in the atmosphere, but to retention of that which is formed in the system, and which, by the ordinary laws of diffusion, cannot be eliminated in an atmosphere of the same gas. The system, in short, is poisoned by a product of its own metamorphosis; and it is to be particularly noted that this product acts, not by a direct toxic action on any one organ, but by putting a stop to the nutritive processes and changes which

result in its own formation, and which processes are essential to the continuance of life. As carbonic acid is formed, not in any one organ, but all over the body, the sudden arrest of its elimination, which occurs when an animal is placed in an atmosphere of that gas, at once puts a stop to the nutritive changes of the whole system, *i.e.*, it puts a stop to those changes whose continuance means life, whose cessation means death.

Carbonic acid, therefore, causes death not by any direct toxic action on this or that organ, but by putting a stop to the nutritive changes of the organs in which it is formed.

Urea is the type of an excretory compound. It is formed chiefly in the liver from retrograde albuminous compounds, and is eliminated by the kidneys. It is the natural stimulant of these organs; and when no disturbing agency intervenes to prevent its elimination, its presence in the blood in undue quantity gives rise to an increased flow of urine.

But disturbing agencies often do intervene, and the kidneys find themselves unable to eliminate all the urea that is formed. It accumulates in the blood; and gives rise to alarming symptoms, chiefly nervous.

These symptoms are noted in connection with Bright's disease, and severe attacks of fever. They were long believed to be due to the direct toxic and irritant action of urea on the nervous centres. It was found in time that urea might exist in excess in the blood, and be injected into the circulation, without causing disturbance of the nervous centres. Impressed with the strength of this objection, Frerichs advanced the hypothesis that the real toxic agent was carbonate of ammonia, produced by decomposition of the urea. But the same objections have been urged in opposition to this view. The existence of carbonate of ammonia in the blood has not been proved, and its competence to produce nervous symptoms, is denied. Oppler thought that the real cause of the nervous symptoms was neither urea nor carbonate of ammonia, but increased metamorphosis of the central organs of the nervous system, and retention in these centres of the products of their own waste. This explanation might apply to cases of fever accompanied by marked nervous symptoms and defective action of the kidneys; but is scarcely applicable to Bright's disease; for there there is no increased metamorphosis. So far, Oppler is no doubt right: it is not so much

retention of urea as retention of excretory products generally, that causes disturbance. The question is, "How do they do so?" If urea, the chief of excretory compounds, produces no direct toxic action on the nervous centres, it is not likely that any other excretory compound would do so.

The only other way in which they can act, is by interfering with the nutritive changes essential to the healthy action of the brain.

These nutritive changes are twofold—constructive and retrogressive. The two advance *pari passu*, and are mutually dependent; interference with either deranging the whole process.

There is abundant evidence to show that defective supply of nutrient material to the brain, gives rise to symptoms identical with those which are noted in connection with retention of excretory products. The severity of these symptoms depends on the extent and suddenness of the deprivation.

In defective nutrition of the brain, resulting from a slowly acting cause, such as improper and insufficient food, long-continued diarrhœa, or other exhausting discharge, the head symptoms are slowly induced, and pass through the various stages of listlessness, languor, irritability, restlessness, mental torpor and confusion, up to a state of wandering and delirium, from which the sufferer may gradually lapse into a state of more or less complete coma.

In the rapidly induced anæmia of the brain, which results from profuse hæmorrhage, from compression of the carotids, or from sudden spasm of the cerebral arterioles, there is no time for the development of the slighter symptoms of defective nutrition; the deprivation of nutrient material is so complete and so rapidly induced, and the resulting cerebral disturbance so great, that it at once gives rise to well-marked convulsions and coma.

The cause of the nervous symptoms in these cases, is defective nutrition of the nervous centres, resulting from defective supply of nutrient material.

But this is not the only way in which malnutrition of the nervous centres may be brought about. Retrograde tissue change is as essential a part of the process of nutrition as constructive; and interference with the former disturbs the whole process as effectually as interference with the latter. It is in this way, and not by any direct toxic action, that

retention of excretory products causes disturbance: the presence in the blood of an excess of these products being, by the ordinary laws of diffusion, a bar to the passage backwards into the circulation of the products of tissue waste, in the same way as an atmosphere of carbonic acid is a bar to the passage outwards of that gas from the system.

Retention of urea and other excretory products in the blood, acts on the tissue respiration in the same way as retention of carbonic acid. The excreta which are in the blood, exercise no direct toxic action on any organ: they simply put a stop to the ordinary tissue change, and so arrest the whole process of nutrition. The brain is the organ which suffers most from such malnutrition: nervous symptoms are, therefore, the first evidence of its occurrence.

The more rapid their accumulation, the more decided the interference with nutrition, and the more marked the symptoms induced.

In ailments, such as chronic Bright's disease, in which they accumulate very slowly and gradually, the severer nervous symptoms which often terminate such cases, are generally preceded for a long time by other minor indications of defective nutrition of the brain, such as we find in starvation, and long-continued exhausting disease—giddiness, headache, irritability, etc. While in acute Bright's disease, and severe forms of fever accompanied by suddenly induced suppression of urine, the disturbance of the nervous centres at once declares itself, just as it does in profuse hæmorrhage and in compression of the carotids, by delirium, convulsions, and coma.

We find, then, that retained excreta exercise two distinct actions: one a stimulant action on the organ by which they are normally eliminated: the other a disturbing action on the tissue which supplies the materials of their formation, when the eliminating organ fails in its duty.

In the light of this knowledge let us proceed to investigate the probable mode of action of lactic acid.

So far as the formation of lactic acid, and the circumstances attendant on it, are concerned, the main fact with which we have to deal is, that its formation in increased quantity is habitually associated with two conditions, (1) active muscular exercise, and (2) rheumatic inflammation of the textures brought into play during such exercise. The question at once arises, "What is the nature of the association?"

In the case of exercise there is not much difficulty in giving an answer. The exercise necessarily precedes the formation of the acid, and the latter must be regarded as a product of the increased retrograde changes which result from the former; that is to say, it is one of the products formed in the metamorphosis of the tissues brought into play during exercise. These are chiefly the muscles with their aponeuroses, the tendons with their sheaths, and the fibrous ligaments of the large joints. We know from the observations of Ludwig and others, already referred to, that increased action of muscle is accompanied by increased formation of lactic acid. The formation of the lactic acid is secondary to the exercise, and to increased activity of the muscular and fibrous textures.

In the case of rheumatic inflammation of the fibrous tissues, the nature of the association is not so apparent. The acid is generally regarded as the cause of the inflammation; and on this view of the matter is based the lactic acid theory of rheumatism. The sole foundation for this view is the existence of the association. But it is quite possible that the association may be the reverse of what is usually supposed—that the inflammation may be primary, and the excess of acid secondary.

Finding that active exercise, which is necessarily accompanied by increased metamorphosis of the tissues of the motor apparatus, causes increased formation of lactic acid; and finding that inflammation of these tissues, which must also give rise to increased metamorphosis, is accompanied by a like increase of acid, it is but natural to infer that in both cases the excess of acid may result from increased retrograde metamorphosis of the tissues. On this view of the matter the excess of lactic acid in acute rheumatism may be secondary to, and consequent on, the inflammation of the fibrous textures characteristic of the disease.

The objection naturally occurs, that a *non-nitrogenous* substance, like lactic acid ($C_3H_6O_3$), is not likely to be formed during the retrograde metamorphosis of a *nitrogenous* structure, like fibrous tissue. And the objection is a valid one. But in studying this question, in considering the various changes likely to take place, and the various substances likely to be formed during the retrograde metamorphosis of the textures involved in acute rheumatism, it is essential that we should bear in mind that, in their function, in their nutrition, in their innervation, and in their vasomotor supply—in short, in all that concerns

their vital activity—these textures are essentially and inseparably connected with the muscles. In all their connections, in all their actions, in all their functions, the muscles, and the fibrous textures involved in acute rheumatism, go hand in hand. Apart from the muscles with which they are connected, the fibrous aponeuroses, the tendons and tendinous sheaths, and the fibrous capsules and ligaments of the joints, have no function, no *raison d'être*. Such being the case, it stands to reason that any change materially affecting their nutritive processes, must be more or less participated in by the muscles.

The muscles themselves may, indeed, sometimes be the seat of rheumatic inflammation, either originating in their structure, or extending to it from the fibrous tissue of the tendons. Such an occasional incident, however, cannot be regarded as adequate to explain a phenomenon of invariable occurrence. It cannot, therefore, be adduced in explanation of that which we are now considering—excess of lactic acid in the blood in connection with rheumatic inflammation of white fibrous tissue.

But independently of the actual occurrence of inflammatory changes in the muscles, it is evident, from the intimate relation which they bear to the textures involved in acute rheumatism, that their nutrition and innervation must be more or less disturbed during the course of that disease. An agency which causes such an increased flow of blood to, and such increased metamorphosis of, the fibrous textures, as occur in the course of acute rheumatism, cannot fail to have a disturbing effect on the vasomotor supply of the whole motor apparatus of the affected joints; and to produce in their muscles some degree of that increased tissue change which is taking place in the fibrous textures. So great are the vascular supply and nutrient activity of the muscles, as compared with those of the fibrous textures, and so important a part are they of the motor apparatus, that it may safely be inferred that, during the course of acute rheumatism, the *actual* increase in their metamorphosis far exceeds that of the inflamed fibrous tissues.

The products of increased metamorphosis formed during an attack of acute rheumatism, must, therefore, be such as would result, not only from increased retrograde metamorphosis of fibrous tissue, but such also as would result from increased retrograde metamorphosis of muscle. That there is increased metamorphosis, and consequent wasting of mus-

cle during acute rheumatism, is evidenced, not only by the increased elimination of urea, but also by the decided wasting and loss of bulk of muscular tissue, noted at the end of the attack.

We have already seen that lactic acid is naturally formed in muscle: and that sarcolactic acid accumulates in it after it has been kept in action.

It is a physiological fact that muscle is one of the chief seats of the formation of lactic acid; and that it is during the retrograde metamorphosis of muscle that it is formed. It is also a physiological fact that the nutrition, innervation, and functional activity of the muscles and fibrous textures of the joints, are inseparably connected, and indissolubly bound up together. It follows from this that inflammation, and consequent increased metamorphosis, of the fibrous textures of the joints, are likely to be accompanied by a corresponding increase in the retrograde metamorphosis of muscle, and consequent increased formation of lactic acid.

The excess of lactic acid which occurs in acute rheumatism, results directly from increased metamorphosis of muscular tissue: this, in its turn, is a result of the disturbance of the vasomotor system of the locomotor apparatus of the affected joints: the cause of this is inflammation of the white fibrous textures of these joints; and the cause of this inflammation is, as already explained, the action of the rheumatic poison.

The rheumatic poison is thus the indirect cause of the presence of an excess of lactic acid in the blood; and this excess thus becomes one of the ordinary phenomena of the disease—one of the necessary results of the rheumatic process.

Reasoning from what we have seen of the mode of action of other excretory compounds, we should expect to find an excess of lactic acid in the system give rise, first, to increased action of the organ by which it is normally eliminated; and, second, to functional disturbance of the textures during whose retrograde metamorphosis it is formed, if for any reason the eliminating organ failed in its duty.

Observation has shown, first, that lactic acid is eliminated chiefly by the skin; and, second, that it is formed during the action and retrograde metamorphosis of the tissues of the motor apparatus.

The effects which we should expect to result from an excess of lactic acid in the blood, are, therefore, increased action of the skin; and,

failing that, functional disturbance of the motor apparatus. And that is exactly what we do find.

Lactic acid is so readily oxidized and eliminated, that it is only in exceptional cases that ingestion can exceed elimination. Hence it is only in exceptional cases that its internal administration can give rise to disturbance. One of these exceptional cases is that recorded by Dr. Foster. The patient was suffering from diabetes and phthisis—both of them ailments accompanied by imperfect oxidation. "In diabetes," says Dr. Foster, "we have a state of disordered nutrition very unfavorable to the conversion by oxidation of new compounds; and in Wright's case this was aggravated by the serious pulmonary complications. Associated with this was a dry branny state of the skin, highly unfavorable to the elimination of the lactic acid by one of the common channels."

Lactic acid given under such circumstances—given, that is, to a man in whose system it cannot be oxidized, and by whose skin it cannot be eliminated—must be retained, and cause disturbance of the nutrition of the textures of whose metamorphosis it is a product. An excess of lactic acid in the blood checks the retrograde metamorphosis of these textures, and so disturbs their whole nutrition, just as retained excreta produces a corresponding action on the brain, and as an atmosphere of carbonic acid interferes with the elimination of that gas from the system.

The symptoms resulting from the retention of lactic acid in the blood are, therefore, likely to be those of functional disturbance of the tissues of the motor apparatus.

Functional disturbance declares itself in different ways in different organs. In the brain it causes nervousness, irritability, headache, giddiness, delirium, convulsions, and coma. In the heart it gives rise to more or less disturbance of the rhythm and force of its action. In the digestive organs it declares itself by evidences of imperfect and deranged digestion. In muscle it gives rise to weakness and loss of bulk. In white fibrous tissue the evidence of its existence is pain, which may be very severe, and is well exemplified by what is felt when a ligament is unduly stretched, or when, as in acute rheumatism, it is the seat of inflammation.

A disturbing agency like lactic acid, which acts on both the muscular and fibrous textures, will declare itself chiefly by symptoms referable

to the latter. It will do so, because these textures give more ready and decided evidence of functional disturbance; and because any weakening of the muscles to which it might give rise, would be lost in the muscular debility and wasting, characteristc of the diabetes for which the acid was given.

Pain, localized in the fibrous tissue, is, therefore, the chief symptom which we should expect to find follow the retention in the blood of an excess of lactic acid. The fibrous tissue which would give the earliest and most marked evidence of disturbance, is that which enjoys the highest degree of functional activity—the ligaments of the large joints. And so in reality it is found to be.

The general result of Dr. Foster's evidence is to show that lactic acid causes increased action of the skin; and, failing this, disturbed nutrition of, and consequent pain in, the fibrous textures of the joints.

But, it may be said, if you grant this—if you admit that excess of lactic acid in the blood may give rise to articular pains—do you not thereby admit the truth of the lactic acid theory of rheumatism? By no means: the two propositions are not only not identical, but are widely different.

That excess of lactic acid in the blood is the cause of some of the phenomena of acute rheumatism, is a position which I not only admit, but am prepared to maintain. But that is a very different thing from saying that it is the exciting cause of the disease, the *fons et origo mali*, which is what the lactic acid theory asserts.

That theory is, that lactic acid is *the rheumatic poison*, the special *materies morbi* which initiates and sets agoing all the phenomena of the disease. One of the most constant of these phenomena is the presence in the blood of an excess of lactic acid. But lactic acid cannot be the cause of its own increased formation—of its own excess. The position is an absurd one; but its very absurdity serves to demonstrate the weakness of the lactic acid theory, and to bring before us the real nature of the question which we have to consider, and of the difficulties we have to face.

The advocates of the lactic acid theory have taken one of the phenomena of the disease, and have raised it from its normal and subordinate position of a symptom, to the rank and dignity of an exciting cause. In so doing they have necessarily fallen into error. Excess of

acid may cause joint pains, but what causes the excess of acid? That has to be explained, no less than the phenomena which combine with it to form the symptoms of acute rheumatism.

And herein we see the inadequacy of Dr. Foster's observations to throw light on the ultimate pathology of the disease; and the short-sightedness of the view which regards them as doing so. In his cases the lactic acid was given to the patient, and its presence in excess was readily accounted for. In acute rheumatism the excess of lactic acid is the phenomenon which, of all others, it is at once most essential and most difficult to explain.

If the first requisite to the production of rheumatism be an excess of lactic acid, the first requisite to a satisfactory theory of rheumatism, is that it should account for this excess.

An attempt to do so has been made by some of the advocates of the lactic acid theory, notably by Corrigan and Senator.

Lactic acid, they say, is formed during muscular exercise. Under ordinary circumstances it is partly oxidized and got rid of as carbonic acid and water; partly, when there is a great deal of it, excreted unaltered in the sweat. Should the cutaneous surface be chilled, the elimination of the acid will be checked, and it will accumulate in the system.

This argument does not stand the test of examination. That chilling of the surface when heated by exercise may be followed by a rheumatic attack there is no doubt. But to be heated by exercise is so common at the age at which acute rheumatism chiefly occurs, and to be exposed to cold so common in the climate in which it most prevails, that a certain allowance must be made for the elements of chance and accidental coincidence.

But making allowance for these, it is probable that overheating and subsequent exposure to cold, and even such exposure without previous overheating, do in some cases seem to determine a rheumatic attack. But it does not follow that the determining agent is the checking of the action of the skin. Overheating and chilling are not the only effects of exercise and subsequent exposure; they are not even the most common. A more constant and more important one is exhaustion; and the probable explanation of the connection which obtains between the exercise and the rheumatism, is that the exhaustion consequent on the former renders the system more susceptible to the action of the poison

of the latter. The depressing influence of cold would lead to the same result.

A greater liability to the action of certain morbific agencies, when the system is exhausted, or depressed from any cause, has been noted in connection with many diseases. Referring to malarial fevers, with which, as we shall by-and-by see, rheumatic fever has many analogies, Niemeyer says, "Exhausting exercises and other debilitating influences, errors of diet, and particularly catching cold, increase the predisposition so much, that persons who have long been exposed to malaria with impunity, are not affected by it till one of these causes has acted on them."

It is the same with rheumatism. It is not the exercise, but the exhaustion which follows it; it is not the chilling of the surface by cold, but the depressing action of cold on the system, which we must regard as the predisposing agencies to the action of the rheumatic poison.

There are other cogent reasons for rejecting the view, that chilling of the surface plays the part attributed to it in the production of acute rheumatism. In the first place, it is to be noted that chilling of the surface when heated by exercise, is frequently had recourse to with impunity, if not with actual benefit. Then again, if we regard sudden chilling of the surface as a danger, and as a cause of acute rheumatism, how are we to explain the beneficial action of the cold bath in the hyperpyrexia of malignant cases of that disease? Here we have the malady presenting itself in the most severe form: lactic acid is being freely thrown off by the skin; the patient is in imminent danger; and yet the only thing which does him good—the only thing which seems to give him a chance of recovering—is to put him in a cold bath, thereby not only lowering the temperature, but checking also the action of the perspiring skin. The same agency which is blamed for causing the patient's illness, is applied in a more decided manner to get him out of it, and is really the only reliable means of attaining this end.

This explanation of the mode of production of acute rheumatism, and of the operation of cold, has other inherent weaknesses. If the argument, as usually stated, means anything at all, it means, first, that during half an hour's violent exercise there is formed in the systems of those of rheumatic constitution, enough lactic acid to produce an attack of acute rheumatism; second, that every time they take active exercise,

such persons are liable to be laid up by that disease; and third, that they are saved from such a misfortune only by the free action of their skins.

But still more is involved in this belief; for if we adopt it, we must also believe that during half an hour's violent exercise there is produced in the system enough lactic acid, not only to give rise to acute rheumatism, but to keep up the symptoms of that disease for weeks and even months, and to supply at the same time the excess of acid which is being eliminated during the whole period of the continuance of the malady.

The mere statement of what is involved in this belief suffices to condemn it. For to suppose that the whole of the lactic acid which is required to produce an attack of acute rheumatism of six weeks' duration, with its accompanying profuse acid perspirations, its hyperacid urine, and acid saliva, could be produced in the system in the course of half an hour, is to presuppose the existence in the system at the end of that half-hour, of a quantity of lactic acid which (granting that acid to be the cause of the rheumatism) would produce the most acute inflammation of all the fibrous tissues of the body, and kill the patient by such inflammation in two or three days. On this view of its causation, every case would be malignant, and death the almost invariable result.

Again, if the poison of the disease were thus produced—if the whole of the *materies morbi* existed in the system at the commencement of the attack—which would be the case if the above view were correct—we should find the symptoms of acute rheumatism developed, not gradually as is the case, but quickly, and very soon after the chill was applied; we should have the joints affected, not in succession as is the case, but all at the same time, and also very soon after the chill; and we should have the heart involved in every case. We should find, too, that the free action of the skin, and consequent elimination of the acid, which characterizes the disease, would be followed by relief of the pain; and that we know is not the case.

No, it is simply impossible that the gradual onset of the symptoms of acute rheumatism, the protracted and varying course of the disease, the shifting character of the joint inflammation, and the long-continued hyperacidity of the secretions, can result from such an excess of lactic acid as could be produced in one, or in a dozen hours' violent exercise.

In an attack of acute rheumatism there is eliminated by the skin alone in twenty-four hours, a quantity of acid greater than is likely to exist in the system at the end of an hour's exercise.

It is erroneous and misleading to regard the excess of lactic acid, which undoubtedly does exist in acute rheumatism, as simply an accumulation. The use of this term, and the undue importance attached to the operation of cold, have led to a misinterpretation of the phenomena observed. What we mean when we say that lactic acid accumulates in the system, is that it is being formed but not properly eliminated. But in acute rheumatism there is increased elimination, as well as increased formation; and this increased elimination goes on during the whole course of the malady. The most severe cases, those in which there is most suffering, and most of the characteristic joint affection, are also those in which the perspiration is most profuse and most markedly acid; and in which, therefore, the acid is most freely eliminated. We cannot say that in such circumstances there is any accumulation of lactic acid in the system. For it is being eliminated in unusual quantity. Such increased elimination implies, not accumulation, but increased formation; and *this* is the phenomenon which calls for attention and for explanation.

Increased formation of lactic acid is a primary and essential feature of acute rheumatism; and no theory of that disease can be regarded as satisfactory which does not recognize and account for this increased formation. This the lactic acid theory fails to do.

Other symptoms of the disease, too, the lactic acid theory not only does not explain, but does not even take cognizance of.

In advancing a theory of the causation of acute rheumatism, we have to account, not only for the occurrence of the joint pains, the febrile disturbance, and the acid sweats, but for the occurrence of the symptoms which precede these special and characteristic manifestations of the fully developed disease; and precede even the evidence of the existence of an excess of lactic acid. A case of acute rheumatism does not leap at once *in medias res*. The characteristic symptoms of the disease are preceded often for two, three, or more days by rigors, shivering, *malaise*, and such aching of the limbs as frequently usher in other febrile attacks. These initial symptoms are as much a part of the ailment as the joint pains which they usher in; and have equally to be

accounted for. This the lactic acid theory does not even attempt to do. It simply recognizes the existence of an excess of acid, and says nothing as to the causation of the phenomena which precede the evidence of its existence.

On this ground alone the lactic acid theory might be rejected. When, along with this, we find, as we have found, that the arguments adduced in its favor can be readily refuted; and that these, its only supports, are no longer available, we can have no hesitation in laying aside this theory, and in rejecting its claim to afford an adequate explanation of the phenomena of rheumatic fever.

But while we reject the view which regards lactic acid as the cause of rheumatic fever, as the morbific agency which originates the disease, we are far from regarding that acid as without action, and as having no share in the production of the phenomena of a rheumatic attack. An excess in the blood of any product of retrograde tissue metamorphosis could scarcely be without some action.

There can be no reasonable doubt that the profuse perspirations which form a characteristic feature of the disease, are due, in part at least, to the stimulant action on the skin of the excess of lactic acid in the blood. It is probable, too, that should formation exceed elimination, the resulting excess of acid would tend to exaggerate the already existing disturbance of the fibrous tissues, and so aggravate the pains and general symptoms of the malady.

We shall by-and-by see that there is reason to suppose that cases in which the fibrous tissues have been weakened and rendered irritable by frequently repeated rheumatic attacks, may have their convalescence retarded, and the ailment prolonged, by the action of the acid on the altered fibrous tissues. Such cases may be placed in the same category as that related by Dr. Foster. They tend to show that the presence of an excess of lactic acid in the blood has a disturbing action on the fibrous tissues; but they do not show that that acid is the rheumatic poison.

CHAPTER VII.

THE MIASMATIC THEORY OF RHEUMATISM.

Lactic acid is the only product of tissue metamorphosis—the only poison produced within the system—which has been specified as being capable of causing acute rheumatism, or as being even available for the purpose. And so no doubt it is. There is no other product of tissue metamorphosis, or of mal-assimilation, to which the rheumatic symptoms can be ascribed.

In rejecting the lactic acid theory we, therefore, reject in its entirety the view which regards the poison of rheumatism as being something which is generated within the system. We are thus thrown back on the only alternative view, that the rheumatic poison enters the system from without.

Of such poisons there are two kinds—the contagia, and the miasmata.

Regarding the nature and mode of action of these poisons, we judge, not by an examination of the poisons themselves—for they have hitherto escaped detection,—but by the phenomena to which they give rise, and the circumstances under which the maladies which they induce are apt to occur.

The essential properties of the contagia are as follows:—

1. They enter the system from without.

2. They are reproduced in, and given off from, the system during the course of the maladies to which they give rise.

3. These maladies are communicable from the sick to the healthy.

4. They have a fixed and definite period of duration.

But rheumatism has no fixed period of duration; it is not communicable from the sick to the healthy; and there is no evidence that its poison is reproduced in, and given off from, the system. The rheumatic poison, therefore, does not possess the properties of a contagium. There remain only the miasmata.

Of the nature of these we have no precise knowledge. Their existence is known to us only by their effects. The poison has never been

separated: and examination of soil, water, and air, supposed to contain it, has given only negative results. What we believe regarding them must be inferred from facts observed in connection with the diseases to which they give rise.

In studying malarial diseases, the facts which force themselves most prominently on our attention are as follows:—

1. They are specially apt to occur in low-lying damp localities, in certain climates, and at certain seasons of the year.

2. Some people are more liable to be attacked than others.

3. They have no definite period of duration.

4. They are not communicable from the sick to the healthy.

Now we cannot fail to see that these are quite the attributes of acute rheumatism. It is most common in temperate climates, at certain seasons, and in damp, low-lying localities. It has no fixed period of duration. It is not communicable from the sick to the healthy. Some people are more liable to it than others; and its poison, we have seen reason to believe, enters the system from without.

But the analogy between rheumatism and malarial disease does not end here. A still further analogy may be traced in their symptoms.

1. Malarial fever is irregular in type, and characterized by variations in its course. So is rheumatic fever.

2. One attack of malarial fever is said to render the system more liable to its recurrence. The same has been said of rheumatic fever.

3. Malarial fevers often leave an impress on the system, which renders the sufferer liable to disturbance and the recurrence of some of their symptoms from slight causes. Rheumatic fever often has the same effect.

4. Unless arrested by treatment, malarial fevers may have a protracted and uncertain course. So may rheumatic fever.

5. The course of malarial fever is speedily arrested by large doses of the cinchona compounds. The course of rheumatic fever is as speedily checked (as we shall by-and-by see) by large doses of the salicyl compounds.

It is evident that the rheumatic poison, both in its history, and in its effects on the system, bears a closer analogy to the poison of malarial fevers than to any other morbific agency.

The poison which gives rise to malarial fever, and that which gives

rise to rheumatic fever, are distinct and separate agencies. But the analogies noted in the natural history and course of the ailments which they respectively produce, are sufficiently close to warrant us in regarding them as generically allied, though specifically distinct.

The poison of malarial fever and the poison of rheumatic fever, are as distinct as those of any two of the specific fevers. But there are many analogies between them; and as good reason for regarding them as similar in nature.

The symptoms, of course, and pathological lesions of rheumatic fever, do not differ from those of intermittent and remittent fever, more than do the symptoms, course, and pathological lesions of typhoid fever from those of small-pox and of relapsing fever. We do not allow the difference in the maladies produced to blind us to the fact that the poisons of small-pox, of relapsing fever, and of typhoid fever, are similar in nature and in mode of action. The differences noted between malarial fever and rheumatic fever at the bed-side and in the *post-mortem* room, need be no hindrance to our regarding their poisons as possessed of like analogies.

The existence of some points of analogy between intermittent and rheumatic fever did not escape the notice of some of the older observers.

Haygarth "thought that there were several analogies between an ague and a rheumatic fever. In both diseases the urine lets fall a similar lateritious sediment. In intermittent as well as rheumatic fever the blood when let is covered with an inflammatory crust. The pain and fever of rheumatism have certain periodical, though not quite regular, paroxysms and intermissions."

The more the natural history of rheumatism is studied, the more apparent become the analogies between it and the common malarial fevers.

Acute rheumatism is generally regarded as a continued fever. But, except its prolonged duration, it possesses none of the characteristics of such a fever.

The continued fevers have a regular and continuous course, a typical and characteristic range of temperature, and a definite period of duration. Often they terminate by a distinct crisis.

Rheumatic fever has none of these characteristics. Its course is irregular. It has no definite period of duration; and no typical range

of temperature. It never terminates by a distinct crisis; and it is impossible to say how long a case may last, if left to pursue its natural course.

Seeing a man suffering from one of the continued fevers, one can foretell with tolerable certainty the future course and duration of the malady. In rheumatic fever this cannot be done. To-day the temperature may be 104°, and the joints acutely inflamed; a couple of days later the temperature may be 100°, and the joints much better. A few days afterwards the acute symptoms may have again returned, and the fever be as high as ever. And so it may rise and fall, and rise and fall, every few days for several weeks in succession; or the disease may come to a termination at the end of eight or ten days; or it may be months before the pain vanishes.

Irregularity is the prominent feature of both the course and the duration of acute rheumatism. "Irregular pyrexia is joined with irregular perspirations." (Scudamore).

It is evident that this fluctuating course is more like that of remittent and intermittent, than that of the continued fevers.

Indeed, like the common malarial fevers, rheumatic fever may be divided into two kinds, *remittent* and *intermittent*. Pathologically they are one and the same disease; but for clinical purposes it is well that a distinction should be drawn between them.

Remittent rheumatic fever is the common acute form of the disease. It is generally regarded as a continued fever; but, as has just been observed, it does not possess the essential features of such a fever. Its characteristics are irregularity of the temperature range, and the shifting character of the joint affection. The joints first involved in the disease are not inflamed all through its course; fresh ones are every now and then invaded. The number of joints inflamed, and the severity of the inflammation, vary from time to time. But the patient is never free from pain or fever during the continuance of the malady.

The whole attack is to be regarded, not as one continuous seizure, but as a series of short ones, which succeed each other so rapidly that the one overlaps the other, leaving no interval between them.

The onset of each individual seizure is characterized by a rise of temperature, and either the invasion of one or more fresh joints, or the

renewal of the inflammation in those already affected; its decline, by a fall of temperature and diminished pain and swelling of the affected joints.

The general course of the malady is the same as in remittent fever; only the remissions and exacerbations are not so regular. It will by-and-by be seen that the explanation of the occurrence of these remissions and exacerbations, is the same in both.

Remittent rheumatic fever is generally acute at the commencement. It occurs in those in whom the rheumatic constitution is very marked, —the same natural peculiarity which leads to a severe attack, leading also to the invasion of fresh joints before those first affected have recovered.

Intermittent rheumatic fever is characterized by an interval of freedom from fever and pain between the two or more seizures which make up its whole course. Instead of running into and overlapping each other, as in the remittent form, they are separated from each other by a clearly marked interval of apyrexia.

The general course of events is the same as in intermittent fever; only the intermissions and the febrile seizures are not so regular.

Intermittent rheumatic fever is generally subacute during its whole course. The rheumatic constitution is not so pronounced as in those who suffer from the more acute remittent form. The inflammation, therefore, is less severe, and new joints are more tardily invaded.

Cases of the remittent form may become intermittent as they begin to decline.

The variations in the course of acute rheumatism here referred to, have been noted by nearly all writers on the subject. They are generally regarded merely as irregularities. Dr. Southey has been more definite; and has described two forms of rheumatic fever—the continued, and the relapsing. But both clinically and pathologically these terms are less accurate and satisfactory than remittent and intermittent: for, in the first place, even in its severe forms, acute rheumatism never is a continued fever, in the sense that that term is usually employed in medicine; in the second place, the term intermission, more aptly than relapse, describes the course of events in the milder form of the disease; and in the third place, remission and intermission convey a definite pathological idea with regard to the nature of the disease; while the

terms continued and relapsing, as applied to acute rheumatism, convey either no pathological view, or one which is erroneous.

The grounds already advanced, suffice to show that there is reason to regard rheumatism as malarial in nature; and its poison as a miasm which enters the system from without. The further prosecution of an inquiry in this direction, necessitates a preliminary investigation into the nature and mode of action of malarial poisons generally.

CHAPTER VIII.

THE NATURE OF MALARIA.

Of the nature of malaria we have no certain knowledge. Its existence is known to us only by its effects. The diseases which constitute the most common and most striking of these effects, are the various forms of intermittent and remittent fever.

These maladies prevail chiefly in marshy localities, in which there is much decomposing vegetable matter. Whatever puts a stop to this decomposition, seems to arrest the development of the miasmatic poison. Cold weather, the complete drying up of the marsh, its drainage, its submergence under water during a very wet season, seem to have the effect of checking the spread of malarial diseases. These are exactly the circumstances which would check vegetable decomposition.

Marshes situated near the sea, and liable to be occasionally inundated by it, are more malarious than those which have no admixture of salt water. The reason given for this is that the salt water kills the fresh-water plants. The marsh thus contains more decaying vegetable matter than it would contain if it were always fresh.

Malarial diseases are most common in autumn, when the vegetable matter formed during the summer begins to decay, and while the heat necessary to its decomposition still prevails.

The association of malarial disease with vegetable decay is undoubted. What is the nature of the association? and how is it to be explained?

Finding this association all but invariable, the conclusion was not unnaturally drawn that the malarial poison was a product of vegetable decomposition, and various gaseous products of such decomposition have been suggested as possibly constituting the toxic agent. It has been found, however, that not one of these produces malarial disease.

Many marshes, too, contain much decomposing vegetable matter, and present all the conditions which have been indicated as necessary

for the development of malaria, without being a source of malarial disease. Where malaria prevails, vegetable growth and decomposition are generally abundant and active. But the converse does not hold: for vegetable growth and decomposition may be abundant and active in a locality which is not malarious.

No product of vegetable decomposition has been proved to be competent to cause intermittent or remittent fever; and no causal connection has been established between vegetable decay and the occurrence of these maladies.

But there is another view of the matter—another possible explanation of the association of vegetable decay with malarial development.

We have seen that intermittent and remittent fevers are most common in autumn, when vegetable decay is most abundant. This is the reason why a causal relation has been supposed to exist between the two. But decay is a mere sequence of death; and death simply the cessation of vital activity. Autumn marks the time at which the annually recurring active growth of plants naturally comes to an end. The increased prevalence of malarial disease in autumn, is thus associated with the cessation of the growth of living, as much as with the onset of the decay of dead, vegetable matter: and it is quite possible that the association may be with the former, rather than with the latter —that the arrest of the processes which constitute vegetable activity, may have more to do with the development of malarial diseases, than has the occurrence of the changes incident to vegetable decay.

The action of salt water may also be thus explained: in killing fresh-water plants, it puts a stop to their vital activity, and to their action on their environment.

Malaria exists in the ground, emanates from it, and infects the atmosphere in its neighborhood. Of this there is ample evidence.

1. The diseases to which it gives rise are associated with certain conditions of the soil.

2. Such disturbance of the ground as cultivation implies, often leads to their occurrence.

3. The poison does not operate at more than a certain height above the sea-level.

4. People who sleep near the ground are more apt to suffer than those who are more elevated.

A poison which is in the ground, and which infects only that part of the atmosphere which is near the ground, has its seat in what may be called the vegetable tract. The chief area of malarial infection, is the area of vegetable influence. The ground in which the roots are, and the atmosphere in which the stem and leaves are, represent the chief seats of the malarial poison.

Now, supposing this poison to be something which may be taken up and absorbed by plants during their growth (and, be it gaseous, liquid, or solid, such a supposition is quite admissible), it is evident that less of the poison would be spread abroad, and be available for the production of disease, during spring and summer, when vegetation is active, than in autumn, when the cessation of growth would leave much of it free. While the cold of winter might temporarily check, or even destroy it. Thus the autumnal development of malarial fever may be casually associated with the autumnal cessation of active vegetable growth.

Evidence in support of this view is found in the purifying effect of vegetation on a malarial atmosphere, as testified to by some facts noted in connection with the natural history of intermittent and remittent fevers.

The marsh poison is carried about in air currents, and may thus give rise to malarial disease at some distance from its home. These malaria-laden breezes may be robbed of much of their deleterious properties, and rendered comparatively innocuous, by having to pass through a belt of trees. On the other hand, the cutting down of trees has been followed by the development of intermittent and remittent fevers in localities which have thus been opened up, and exposed to direct currents from a malarious district.

It is claimed, too, for some trees and plants, and that not without some show of reason, that they possess the property of removing malaria and rendering a district more healthy. The one quality common to all the trees and plants which have been so commended, is rapidity of growth, and, therefore, great activity of the nutritive processes.

We know that malaria may be taken into the system of man, either through the lungs, or, in drinking water, through the digestive organs. There is no reason why it should not be absorbed by plants, either in water through their roots, or from the atmosphere through their leaves,

or by both channels. This is probably the mode in which trees exercise their purifying effect on malarious atmospheres. The cessation of their growth in autumn is the probable reason why malarial fever is most prevalent at that season. The malarial poison may be as abundant in summer; but the active state of vegetation at that season, leads to the absorption of much of it by the leaves and roots of plants, and to its consequent destruction as a morbific agent. In other words, malaria seems to be developed during the hot season; but chiefly at the latter part of that season, when ordinary vegetation ceases to be active, does it have full scope for its disease-producing powers.

Again, malarial atmospheres are more deadly during night than during day. The literature of the subject abounds with instances in which the members of a ship's crew who went ashore in a malarial district only during the day, escaped, while those who remained ashore all night, suffered from malarial fever. This deleterious effect of night air is well known to dwellers in malarial districts, who, during the day, go freely and with impunity into places which they would not think of visiting during the night. No satisfactory explanation has been given of this. It has been supposed to be due to chilling of the body by the night air; but the night may be oppressively hot, and the result be the same as if it were cold. It has been attributed to lowering of vitality during sleep; but sleep may be indulged in during the day with impunity; and being awake at night, does not protect from danger.

Dr. Mitchell,[1] who strongly and ably advocated the view that malarial poisons were allied in nature to the fungi, thought that, like fungi, these poisons were developed only during the night. "When we observe the extraordinary tendency of fungous vegetables to develop their power only at night, we detect *another analogy between malaria and the fungi*. In vain do we search in the latter part of a day for young mushrooms. A field which at evening exhibited not a single plant, is often whitened by their little umbrellas in the morning. . . . . Supposing the minutest fungi to possess the general properties of the class to which they belong, we may readily perceive what prodigious influence must be exerted on them by the damp rich air of a swamp."

[1] On the Cryptogamous Origin of Malarious and Epidemic Fevers, by J. K. Mitchell, A.M., M.D., Professor of Practical Medicine in the Jefferson Medical College of Philadelphia. Lea and Blanchard (1849).

Another explanation of the deleterious effects of night air is, that vapors which are dissipated abroad during the day, are again condensed near the ground at night; and that such vapors are apt to retain the malarial poison in them.

Both these views may contain an element of truth. But they do not explain the purifying effect of vegetation on a malarial atmosphere. Another factor is almost certainly at work.

If the view which has been advanced as to the mode in which trees act as purifying agents on a malarial atmosphere be correct, it necessarily follows that this action must be less during night than during day; for night is the time at which leaves cease to perform their absorbent function; and at which, therefore, they cease to exercise a purifying influence on a malarial atmosphere.

The facts with which we have to deal are—

1. That malarial fevers increase in prevalence when vegetable growth ceases to be active.

2. That malarial atmospheres are most deadly at night.

3. That growing trees exercise a purifying effect on such atmospheres.

It seems to me that the view which best fits into, and explains, these facts, is that which regards the marsh poison as something which may be taken up by the leaves and roots of plants, in the ordinary performance of their nutritive function. Such a view does not exclude from consideration the operation of the other agencies to which reference has been made.

But still the question remains, What is the nature of this poison?

The old view that it was a gaseous product of vegetable decay cannot be accepted; for such products have been shown to be incompetent to cause malarial fevers. Vegetable decay is abundant in many places where malaria is unknown; and malaria abounds where there is little or no decaying vegetable matter.

The opinion most generally entertained now-a-days is that the malarial poison consists of minute organisms. "I have no hesitation," says Niemeyer, "in saying decidedly that marsh miasm—malaria—must consist of low vegetable organisms." Though the evidence is scarcely sufficient to warrant so strong a statement, there can be no doubt that this is the view which best accords with the

phenomena noted in connection with the origin and spread of malarial disease.

The usual objection to this view is that, if such were the nature of the poison, its existence could be demonstrated by the microscope. But that by no means follows. The microscope can demonstrate the existence of very minute organisms; but beyond a certain point it cannot go. And it has to be borne in mind that the limit to microscopic demonstration of such minute objects, is not so much the mechanical power of the microscope, as the visual power of our eyes. An object may be magnified 30,000 times and be visible; and yet disappear from the field of our vision when magnified 60,000 times. The object is there, but its image is so attenuated by the increased power of the microscope, that our eyes can no longer detect it. Professor Tyndal has demonstrated that the atmosphere habitually teems with particles so minute that they cannot be detected by the highest powers of the microscope, and that many of these particles are organized. With the knowledge that organized particles so minute do exist, we cannot fail to see that our inability to demonstrate that malaria is particulate and organized, is no proof that such may not be its nature.

Certain it is, that this view is the one which best explains the phenomena with which we have to deal. Adopting it, we can at once see (1) why a damp locality favors the development of malarial fever; for moisture is favorable to the development of organized life: (2) why the drying up of the soil, and the onset of cold weather lead to an opposite result; for such conditions check the growth of organisms: (3) why complete flooding of a marsh has the same effect; for such an event puts a stop to direct communication between the soil and the atmosphere. (4) This view gives also an adequate explanation of the purifying effect of growing plants and trees on a malarial atmosphere. If malaria is organized, the organisms of which it consists are so excessively minute that they have hitherto escaped individual detection; they are, therefore, probably not more than $\frac{1}{30000}$th of an inch in diameter. To the absorption of such minute particles by the roots and leaves of plants, there is no obstacle.

The researches of Lanzi and Terrigi,[1] and the more recent ones of Professor Klebs and Signor Tommasi-Crudeli,[2] made in the malarial

[1] Centralblatt, f. Med. Wiss. 1875. [2] Allg. Wien. Med. Zeit. 1879.

district of the Agro-Romano near Rome, point to the conclusion that the malarial poison is an organism which may be obtained from the soil, and may be cultivated in the bodies of animals. This organism, say the last two observers, belongs to the genus bacillus, and exists in the soil of malarial districts in the form of shining ovoid spores; to it they propose to give the name of *bacillus malariæ*. By inoculating rabbits with liquids taken directly from malarial soil, and containing this bacillus, there was produced fever, often of an intermittent type. Another result of such inoculation was enlargement of the spleen.

It is apparent that the balance of evidence and of authority favors the view that malarial poisons are minute organisms. Such being the case, we shall assume that they are so; and shall proceed to investigate the probable mode of action of such organisms on the system. For if this view of their nature be correct, the phenomena to which they give rise in the system must be such as an organism would produce; and a detailed consideration of these phenomena will tend to throw light on the true nature of the poison which causes them.

CHAPTER IX.

THE MODE OF ACTION OF MALARIA.

Malaria may act like ordinary medicinal and poisonous agencies; it may act after the manner of a contagium, and have its action intimately connected with organic development; or its mode of action may be altogether peculiar.

To say that malaria acts like ordinary medicinal and poisonous agencies, is not to explain its mode of action; for of the manner in which many of these produce their effects, we know little or nothing. We know that opium contracts, and belladonna dilates, the pupil; that ergot stimulates the uterus; that cantharides acts on the bladder, and arsenic on the stomach and rectum. But why each of these agencies has its own special action: why belladonna never contracts the pupil: why the action of cantharides is specially on the bladder, and that of arsenic on the stomach and rectum, we do not know. Under these circumstances we cannot expect to learn much of the mode of action of malaria from a study of the effects of ordinary medicinal agencies.

Malaria differs, too, so widely from such agencies, both in its nature, and in the effects to which it gives rise, that it is likely also to differ from them in its mode of action.

That contagia are organisms, and that their morbific action is intimately associated with, and dependent on, their organic growth, are propositions which I have elsewhere[1] considered and maintained in some detail. The evidence in support of this view may be briefly summed up as follows:—

1. The effects produced in the system by a given contagium, bear no relation to the quantity administered—a small dose acting, if it act at all, as vigorously as a large one.

2. During its action the poison is largely reproduced in the system.

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[1] The Germ Theory applied to the Explanation of the Phenomena of Disease, by T. J. Maclagan, M.D. (Macmillan & Co., 1876).

3. The quantity eliminated from the system is always greatly in excess of that received into it.

4. The locality in which its action is most marked—the seat of the local lesion in the eruptive fevers, for instance,—is also that in which the poison exists in largest quantity.

5. The action of the poison ceases, while the system contains a much larger quantity of it than sufficed to cause the disease to which it gives rise.

6. The maladies produced by the contagia are communicable from the sick to the healthy.

The existence of such peculiarities, creates a broad line of demarcation between contagia and ordinary medicinal agencies.

They also separate them from malaria: for in malarial disease there is not the same evidence of organic reproduction; there is no evidence of elimination of the poison; and malarial fevers are not communicable from the sick to the healthy.

The question of the mode of action of malaria is, indeed, beset with peculiar difficulty; for (unless, possibly, in the experiments of Klebs and Tommasi-Crudeli already referred to) the poison has never been separated, and experimented with.

In the case of ordinary medicinal agencies we have the substance itself, the agent whose action we are investigating, in our hands, and under our eyes. We can administer it in any way, in any quantity, and under any circumstances. With some of the contagia, too, we can separate the poison, regulate the dose, and study the effects under various circumstances; and from what is observed in these, may be drawn inferences applicable to the whole of the contagia.

If, with all these advantages, we are still lacking in information regarding the manner in which medicinal agencies and contagia produce their effects,—if with the poisons at our disposal, and ready to our hand for experimental investigation and research, we can come to no satisfactory conclusion regarding the manner in which they act,—can it be wondered at that we should know nothing as to the mode of action of malarial poisons, which have never been separated, and have never had their existence recognized, except through the maladies to which they give rise?

If the malarial poison is an organism—and the evidence all favors the view that it is so,—it is more likely in its mode of action to resemble contagia than ordinary medicinal agencies. It is to be noted, as evidence in support of such a view, that the phenomena to which it gives rise in the system, are more analogous to those resulting from the action of contagia, than to any effects produced by ordinary poisons and medicines.

Contagia and malaria are both intangible agencies introduced into the system from without. Both are associated with bad hygienic conditions. Both have for the most striking of their effects on the system, the occurrence of idiopathic fever. In each the fever is specific in nature; in each it has a more or less distinctive course.

But still further analogies may be traced. The continued fevers to which the contagia give rise, are divided into two classes, the eruptive and the non-eruptive. The former are represented by typhus, typhoid, scarlet fever, measles, small-pox: the latter by relapsing fever.

Malarial fevers may also be divided into two similar classes, the eruptive and the non-eruptive. The latter are exemplified in intermittent and remittent fevers: the former in rheumatic fever.

The distinction between an eruptive and a non-eruptive fever is, that the latter consists simply of fever: the former of fever *plus* a local lesion. The local lesion of rheumatic fever is the joint affection.

The existence of such analogies constitutes a reasonable foundation for the view, not only that malaria is allied in nature to contagium, but that it is also likely to resemble it in its mode of action.

If it act after the manner of a contagium, and owe its effects to its organic development within the system, we shall find evidence in support of this view in a detailed consideration of the phenomena to which it gives rise. In other words, if the poisons which produce the different forms of malarial fever, are organisms whose morbific effects are due to their organic development within the system, the symptoms of malarial fever will be such as would result from the propagation of an organism in the system.

The essential characteristics of the form of fever which is universally regarded as of malarial origin, are its intermitting or irregular course, and its occurrence independently of a local inflammatory cause.

The question which we have to consider is the competence of an organism to produce such a result.

That the reproduction of an organism in the system is capable of producing the essential phenomena of the febrile state, we have, in the case of the continued fevers, shown in some detail.[1]

An organism has for its most distinctive characteristics, the power of organic reproduction and development, and a certain action on its environment. This latter is dependent on the former, and consists mainly in the consumption of nitrogen and water. But nitrogen and water are the very materials required by the tissues of the body. The propagation in the system of millions of organisms having such wants, must lead to an enormous increase in the consumption of these materials. This means simply the development of fever; for such an increase must give rise to quickening of the circulation, increased tissue waste, increased consumption of water, rise of temperature, and increased elimination of urea. This aggregate of phenomena constitutes the febrile state. The propagation in the system of such organisms as we believe malarial poisons to be, is, therefore, competent to the production of the most prominent and essential feature of the maladies to which these poisons give rise—idiopathic fever.

But though there are many analogies between continued and malarial fevers, there are also great and important differences. These, equally with the analogies, call for consideration. They are as follows:—

1. There is ample evidence that the poisons of the continued fevers are reproduced in, and given off from, the system in large quantity during the course of the maladies to which they give rise. There is not such evidence in the case of the malarial fevers.

2. The continued fevers are communicable from the sick to the healthy. Malarial fevers are not.

3. The continued fevers have a continuous, regular course, and a definite period of duration. The course of malarial fevers is intermitting and irregular, and their period of duration indefinite.

4. One attack of the continued fevers confers, as a rule, immunity from a second. There is no such immunity in malarial fever.

Let us consider each of these points separately.

[1] Maclagan, op. cit., p. 34 et seq.

1. *Contagia are reproduced in and given off from the system. Malaria is not.*

The evidence of the reproduction of the poisons of the continued fevers, is their elimination in increased quantity, and in an active form. And the evidence is sufficient. A poison cannot be received into the system in small quantity, and be given off from it in large, without having been reproduced there. But though increased elimination is a proof of reproduction, its absence is not a proof to the contrary. An organized poison might be reproduced in, and exercise its action on, the system without being eliminated in an active form. Its life history might be completed in one cycle of growth within the system, and itself come to an end in the course of the morbid action which it had set agoing. Or it might be destroyed and disintegrated in the system, and thrown off by the eliminating organs. In either case it would pass from the system in a form different from that in which it entered in.

It is certain that in malarial fevers the poison is introduced from without. It is probable that this poison is an organism. If it be so, it is capable of organic growth and reproduction; and its action is likely to have a relation to these processes.

The phenomena of these fevers are indeed such as can scarcely be explained in any other view. A short residence, even one night, in a malarial district, may give rise to a fever of some weeks' duration. If, during one night, the patient inhaled enough poison to cause so prolonged an attack of fever—if the whole of the poison requisite for the production of such an illness, existed in the system at the commencement of the attack, he surely should be killed right off by a dose competent to produce such an illness. Again, if the dose taken suffice to cause the fever, why does it not go on acting? Why are there intermissions and remissions? Why is the patient one day in a raging fever, and the next day free from it? And why, in the absence of treatment, does this alternation of pyrexia and apyrexia go on indefinitely?

In the case of rheumatic fever the same difficulty presents itself. If the whole of the poison necessary to produce an attack of a month's duration exist in the system at the commencement of the seizure, how is it that all the joints do not suffer at once? Why does the local inflammation present intermissions and remissions? Why does the inflammation quit a joint, and, after a time, come back to it? And why, in the

absence of appropriate treatment, does the disease have so prolonged a duration?

If the whole of the poison necessary to the production of all the phenomena of the malarial fevers existed in the system at the commencement of the illness, they would lose their intermittent and remittent character, the full effects of the poison would be produced at once, and their phenomena would be concentrated into one violent attack of fever, which could scarcely be recovered from.

If the whole of the poison of rheumatic fever existed in the system at the onset of an attack of that disease, the symptoms would be developed, not gradually as is the case, but all at once—the joints, instead of being affected by twos and threes, would all suffer at the same time, and the disease would lose some of its characteristic features.

It is impossible to explain the phenomena of the malarial fevers on the supposition that the whole of the poison necessary to the production and full development of each, exists in the system at the time of its onset. Their varying course, their often-increasing severity, their prolonged duration, and their small mortality, can be accounted for only on the view that their poisons are reproduced during the course of the maladies to which they give rise—that that which produces the symptoms of to-day has to-morrow ceased to be active; but has given rise to an offspring which keeps up the action which its parent set agoing; and in its turn hands down to its offspring the same morbific properties which itself received.

Such reproduction is peculiar to organized structures.

That the poisons of malarial fevers are somehow destroyed in the system there can be no reasonable doubt. They enter it from without; they are almost certainly reproduced therein; and they are not eliminated in an active form. They must, therefore, be destroyed and disintegrated. The only alternative view is that they remain permanently in the system; and that is an untenable position.

It seems to me that we must accept the view that malarial poisons are destroyed, probably in some of the eliminating organs, and that the products of their destruction are eliminated with the ordinary excreta. The presence of these products in the system may partly explain the unusually copious urinary deposits which are noted in connection with intermittent, remittent, and rheumatic fevers.

The fact that malarial poisons are not eliminated from the system in an active form, does not prove that they are not reproduced in it.

2. *Malarial fevers are not communicable from the sick to the healthy.*

Communication of a disease means the passage of its poison from the bodies of the sick to those of the healthy. It, therefore, presupposes the elimination of that poison in an active state. Malarial fevers are not communicable, because their poisons are not so eliminated. Non-communicability is at once the proof, and the necessary consequence, of non-elimination in an active state.

3. *Malarial fevers have an intermitting indefinite course, and an irregular period of duration.*

The poisons of the continued fevers and of malarial fevers, if organisms, are also parasites. As such they require for their development something more than the bare materials requisite to organic growth—something which they find in their nidus, and which is as necessary to their reproduction as are nitrogen and water to their organic growth. The materials requisite to organic growth exist all over the body, and are practically unlimited. The special material which the poisons find in their nidus (and which for convenience sake we call the second factor) is not so. It exists only in the nidus, in definite and limited quantity, and may, therefore, be readily exhausted. In typhoid fever, for instance, it is limited to the intestinal glands—in small-pox to the skin. So long as any of this second factor exists, the poison continues to be propagated, and the febrile symptoms are kept up. When it is exhausted, the system no longer possesses the necessary nidus—no longer presents to the poison the conditions requisite to its continued action—its propagation ceases, and the fever comes to an end.

The quantity of the second factor is not the same in all persons. It has an average, however; and the period requisite for using up this average, represents the mean duration of the malady. If the quantity be large, the contagium finds a rich field for its propagation and development, and the resulting attack is prolonged and severe: if small, the field is a poor one, and the resulting attack is short and mild.

The course of the continued fevers is continuous and regular, because the quantity of the second factor in the nidus does not fluctuate; and because, therefore, the contagium goes on being reproduced

steadily, continuously, and without break or intermission, until the nidus is exhausted.

Their period of duration is definite, because the second factors necessary to the propagation of their poisons, exist in limited and definite quantity, are exhausted in a given time, and when exhausted, are reproduced tardily or not at all.

In typhoid fever, for instance, the second factor necessary to the propagation of the poison of that disease, has its seat in the intestinal glands. In the absence of these glands (as in infancy, in old age, and after their destruction during an attack of typhoid) the typhoid poison has no action on the system; it is as impotent for evil as is the poison of small-pox to one who has already suffered from that disease.

At the commencement of an attack of typhoid fever, these glands contain a certain quantity of the second factor. It is evident that this quantity must be both definite and limited. It is because its quantity is definite, and not liable to vary during the course of the disease, that the fever is continuous. It is because it is limited, and is not apt to be reproduced, that the fever has a fixed period of duration.

If there existed a parasitic organism whose second factor, after having been exhausted, was readily and quickly reproduced, before the first factor, the organism, was all eliminated from the system, the fever resulting from the propagation and growth of this organism would consist, not of one continued attack, but of alternations of pyrexia and apyrexia; and as the exhaustion and reproduction of the second factor might go on indefinitely, so also might this alternation. In this way there would be developed a disease having all the characteristics of intermittent fever.

If the second factor were still more rapidly reproduced, it might never be thoroughly exhausted, its quantity might only be considerably reduced, and continue to rise and fall, and rise and fall, for some time, without being quite used up. In this way there would be produced a disease having all the characteristics of remittent fever.

If the second factor, instead of being localized, as it is in the eruptive fevers, existed in the blood, such rapid reproduction would be very likely to occur; for the blood is an everchanging fluid, containing nothing but what, when removed, is likely to be replaced.

That the second factor may exist in the blood, and may be so

quickly reproduced as to give rise to alternations of pyrexia and apyrexia, is evidenced by what we see in relapsing fever.

This is the only one of the continued fevers in which an organism has been detected in the blood. It is also the only one in which the course of the fever is not continuous, and in which there is no characteristic local lesion. With reference to the spirilla which is found in the blood, it has been proved that it exists during the pyrexia, and is absent during the apyrexia, and there can be no reasonable doubt that the spirilla is the poison whose propagation causes the disease.

"The characteristic feature of relapsing fever is the relapse. There is a febrile attack of six or seven days' duration, then a period of freedom from fever of a week's duration, then another febrile attack of shorter duration than the first, and then another period of freedom from fever, which is generally permanent; but there may be as many as four or five relapses. During each period of pyrexia the spirilla is found in the blood: during each period of apyrexia it is absent. The pyrexia we attribute to the growth and propagation of the organism—the apyrexia to its absence. If we can explain the cessation of its propagation, we shall have accounted for the distinctive course of relapsing fever.

"The absence of the spirilla during the apyrexia may be due either to some peculiarity of the contagium, or to some peculiarity of the second factor.

"If the contagium were an organism which naturally went through a series of changes involving alternate periods of activity and repose; and if the phenomena of the febrile state were the result of such changes as occurred only during the period of activity, it is evident that the propagation of such an organism in the system would give rise to a malady characterized by alternations of pyrexia and apyrexia. The spirilla might thus give rise to relapsing fever.

"But if such were the case—if each febrile attack corresponded to the advent of another period of active growth of the parasite, we should probably find some change in its external appearance, some evidence of a further development of the organism. We should probably find, too, that it was present to some extent during the apyrexia. But such is not the case. The spirilla is found only during the pyrexia, and

presents in the second, third and fourth seizures, exactly the same appearance which it presented in the first.

"Again, if such were the explanation of the distinctive course of relapsing fever, we should almost certainly find the course of the malady the same in each case. If the contagium had certain normal stages of development to go through, these stages would always be the same; and the course of the symptoms to which they gave rise would be the same also. But this is not in accordance with fact. The number of pyrexial attacks is generally two; but there may be only one, or there may be three, four, five, or even six.

"For these reasons we conclude that the cause which gives rise to the distinctive features of relapsing fever, is not to be found solely in some peculiarity of its contagium. The only other possible cause is some peculiarity of its second factor.

"The peculiarity of the second factor of relapsing fever is its general distribution in the circulating fluid. Could such a peculiarity induce the phenomenon now before us—a re-accession of fever?

"In the eruptive fevers we attribute the decline of the febrile symptoms to the exhaustion of the second factor. In relapsing fever we attribute their decline to the same cause.

"The permanent duration of convalescence in the eruptive fevers we attribute to the fact that this exhaustion is permanent—that the second factor is not reproduced. The absence of such permanency in relapsing fever we attribute to the opposite cause—the second factor *is* reproduced. The occurrence of the characteristic second seizure of relapsing fever is due to the circumstance that the second factor is reproduced in the blood before the first is thoroughly eliminated from it; its early reproduction leading to the renewed development of such germs as remain, and a consequent second pyrexial attack.

"If such be the explanation of the relapse, it is evident that cases might occur in which, either from more rapid elimination of the first factor, or from more tardy reproduction of the second, the former might be thoroughly eliminated before the latter was reproduced. The consequence would be the absence of the usual characteristic of the disease—there would be no relapse, the attack being completed in one seizure. That such cases do occur is an established fact in the history of relapsing fever. Of 2425 cases collected by Murchison, 724 had no

relapse. Of 100 consecutive cases under Murchison's own care, 4 were completed by one pyrexial attack. Of 400 recorded by Litten, 6 had no relapse.

"Again, if the second factor be so frequently and so quickly renewed, it is evident that the process might be repeated more than once, and that a third seizure might be caused in the same way as the second, and a fourth in the same way as the third; the sole requisite to the production of a pyrexial attack, being the reproduction of the second factor, prior to the complete elimination of the first. Such cases are observed in every epidemic. Of 1500 cases collected by Murchison, a second relapse, *i.e.*, a third pyrexial attack, occurred in 109, or in 1 in 14; a third relapse in 9, or in 1 out of 166; and a fourth relapse in 1 of the 1500. Of Litten's 400 cases 35½ per cent. had a second relapse, while 7 of them had three, and 3 had four relapses. The mode of production of each seizure is the same; the second factor is reproduced before the first is eliminated."[1]

From what we find occur in relapsing fever, we know that the period of pyrexia corresponds to the period of abundant propagation of the organism—the period of apyrexia to its absence.

From what we believe regarding the nature of the poisons of malarial fevers, from a consideration of the phenomena to which they give rise, and from a comparative study of what is observed in the somewhat analogous case of relapsing fever, we regard it as in the highest degree probable, first, that the poisons of intermittent and remittent fevers find the second factors necessary to their propagation in the blood; second, that this second factor is at no time very abundant; third, that it is, therefore, quickly used up during the active propagation of the poison; and fourth, that when used up it is quickly reproduced. The rapid using up and speedy reproduction of the second factors, has much to do with the production, not only of the characteristic intermissions and remissions of these fevers, but also with their equally characteristic indefinite period of duration. Their course is intermitting and irregular, because the quantity of the second factor essential to the reproduction and action of their poisons, fluctuates and varies during the course of this action; and because, therefore, the quantity of

[1] Maclagan, op. cit., page 34 et seq.

poison reproduced varies from day to day. Their period of duration is indefinite, because the tendeney to the speedy reproduction of the second factor is not limited to a definite period of time.

In rheumatic fever the second factor exists, not in the blood, but in the fibrous textures of the motor apparatus.

The functional activity of these textures cannot be impaired without embarrassment, for their duties are important, and cannot be delegated; they, and they alone, can do the work which falls to them. Any change in their composition is, therefore, likely to be temporary.

In the irregular distribution of this second factor, in its tendeney to speedy reproduction, and in the consequent alternations of diminution and increase in quantity, we find an adequate explanation of the characteristic irregular course and duration of rheumatic fever.

In remittent rheumatic fever, as in common remittent fever, the second factor is so speedily reproduced that there is no time for more than a partial declension of fever and pain. They remit, but do not intermit.

In the intermittent form, as in ague, the second factor is reproduced so tardily that the symptoms of one seizure have time to decline, and the temperature to become normal, before the onset of the next. Its reproduction is delayed long enough to permit of the declension of the rheumatic symptoms, but not long enough to permit of the destruction of the whole of the rheumatic poison prior to its renewal. The disease is intermittent for the same reason that it is subacute. The rheumatic constitution is not marked. There is not enough of the second factor to give-rise to an acute attack; and not a sufficiently marked tendency to its speedy reproduction to make the disease remittent.

In the malarial fevers, as in relapsing fever, a time comes when the renewal of the second factor is so retarded, that the poison is all got rid of before that event takes place. The advent of this time marks the onset of convalescence.

4. *One attack of malarial fever confers no immunity from a second.*

The insusceptibility to the action of the poisons of the eruptive fevers, enjoyed by those who have once suffered from them, constitutes one of the most striking characteristics of these maladies.

As the decline of the fever is due to the exhaustion of the second

factor, so immunity from a second attack is due to its non-reproduction. If, after having been exhausted, the second factor be not reproduced, the system no longer presents the conditions requisite to the propagation of the contagium, and it does not act. That such is the explanation of the immunity from second attacks enjoyed by those who have once suffered from these diseases, is evidenced by the fact that, as a rule, no amount of exposure to their poisons, not even their direct introduction into the system, serves to produce a second seizure.

It is to be noted that this immunity is peculiar to the eruptive fevers; that is, to those forms of continued fever in which the second factor is localized in some particular organ: and that relapsing fever, the only one in which the second factor is not thus localized, is also the only one in which one attack confers no immunity from a second. In relapsing fever the second factor exists in the blood.

Now it is evident that a lasting impression may be more readily made on a formed and solid organ, than on a constantly changing fluid like the blood. An organism which finds its second factor in the former is, therefore, more likely to produce a permanent impression than one which finds it in the latter. Moreover, it is to be observed that some of the tissues which are the seat of the local lesions of the eruptive fevers, are apt to undergo permanent change in the ordinary course of nature. I would specially instance the tonsils, which are affected in scarlatina; and the intestinal glands, which are involved in typhoid fever; both of which dwindle away, and ultimately disappear, as years advance.

In intermittent and remittent fevers, the second factor also exists in the blood; and is, therefore, likely to be readily reproduced.

The same tendency to the reproduction of their second factors, which serves to account for the varying course and indefinite duration of these maladies, serves also to explain their tendency to recur again and again in the same individual. The second factor is reproduced; and with its reproduction there is a renewed susceptibility to the action of the first.

In rheumatic fever the second factor exists in tissues whose functions are so important, and so peculiar, that a permanent change is not likely to take place in them during their period of functional activity. The same natural tendency which originally led to the existence of this

second factor in these tissues, leads also to its reproduction, after it has been exhausted during a rheumatic attack.

It is generally said that one attack of malarial fever (intermittent, remittent, or rheumatic) produces a greater susceptibility to its subsequent recurrence. The truth is, that the constitutional peculiarity which led to the first, leads equally to subsequent attacks; and the later as well as the earlier attacks are merely the evidence of the existence of this peculiarity.

We have now given the reasons for our belief, first, that the rheumatic poison is malarial in nature, and therefore allied to the poisons of intermittent and remittent fever; second, that malarial poisons are organisms, and therefore allied to the contagia; third, that they act after the manner of these, and owe their morbific action to their organic development within the system. We have further endeavored to explain the differences noted between the effects produced by these two different classes of poison. In doing all this we have laid a reasonable foundation for a miasmatic theory of rheumatism.

Hitherto we have dealt with malarial fevers generally. It was necessary to the elucidation of our special subject that we should do so. Regarding intermittent and remittent fevers we have said only what was necessary, on the one hand, to explain the etiological relationship which exists between these maladies and rheumatic fever; and on the other, to exemplify the similarity which obtains between the mode of action of their poisons, and those of the continued fevers. In doing so, we have necessarily dealt with phenomena which are common to all forms of malarial fever.

But if the miasmatic theory of rheumatism be correct, and if it be the case that the poison of that disease is an organism whose morbific action is intimately associated with its organic development—we should be able to explain by it, not only the features which rheumatic fever presents in common with other forms of malarial fever, but likewise those which are peculiar to, and distinctive of, it. We should, in short, on this theory be able to explain the whole of the phenomena of the disease.

Those which have hitherto come under our notice are:—

1. The occurrence of fever.

2. The non-elimination of the poison.
3. The non-communicability of the disease.
4. Its varying course and indefinite duration.
5. The liability to repeated attacks.

These are the general phenomena of the malarial fevers, which are noted in rheumatic as in the other forms; and the explanation of which we have endeavored to give.

It remains for us to consider the special features of rheumatic fever, and to explain, on the miasmatic theory, the essential and characteristic phenomena of that disease.

We have seen that rheumatism is essentially a disease of the motor system; and that this motor system consists of two parts, a loco-motor and a vasculo-motor apparatus.

Though no pathological distinction can be drawn between rheumatism affecting the loco-motor and rheumatism affecting the vasculo-motor apparatus; and though neither can be satisfactorily considered without reference to the other; it is, nevertheless, convenient for clinical purposes that a distinction should be drawn between them, and that each should be separately dealt with. Indeed, rheumatic inflammation of the vasculo-motor apparatus is so formidable and so serious a disease, that it demands special and separate consideration.

What we have to say on the general subject of rheumatism shall, therefore, be considered under the two heads of *rheumatism of the loco-motor apparatus* and *rheumatism of the vasculo-motor apparatus*.

CHAPTER X.

RHEUMATISM OF THE LOCO-MOTOR APPARATUS.

ACUTE rheumatism we regard as a form of malarial fever. What we have now to do is to apply this miasmatic theory to the elucidation and explanation of its distinctive phenomena.

These phenomena are:—

1. The occurrence, along with the general febrile disturbance, of a local inflammatory lesion.
2. The almost entire limitation of this lesion to such parts of the motor apparatus of the body as are habitually subject to active movement and strain.
3. The tendency of the disease to attack those of a particular age.
4. Its hereditary transmission.
5. The presence in the blood of an excess of fibrine.
6. The presence in the blood of an excess of lactic acid.
7. The occurrence of profuse perspirations.
8. The shifting character of the joint affection.

These we shall consider in the order enumerated.

1. *The occurrence, along with the general febrile disturbance, of a local inflammatory lesion.*

When dealing with malarial fevers generally, we saw that the course of their febrile phenomena was such as could be explained only on the view that the poison which gave rise to them was reproduced in the system. What was then said on the general subject of malarial fever, applies also to the special subject of rheumatic fever. The special peculiarity with which we have now to deal, is the association with this febrile disturbance of a local inflammatory lesion.

This association occurs under two different circumstances: (1) The inflammation may precede the fever; or (2) the fever may precede the inflammation. In the former case, the fever is the result of the inflammation, and is said to be symptomatic; in the latter, its onset precedes the evidence of local inflammation, and it is said to be idiopathic.

An instance of the former we have in pleuritis or synovitis following cold or injury: an instance of the latter we have in the bowel lesion of typhoid fever, and in the sore throat of scarlatina.

The first evidence of the existence of acute inflammation of fibrous or serous tissue is pain. The first evidence of febrile disturbance is a feeling of cold and *malaise.*

In purely local inflammations, such as those already instanced, pain is the first symptom. Shivering, *malaise,* and general febrile disturbance may quickly follow, or may even be contemporaneous with the pain; but they do not precede it.

In the local lesions of the specific fevers the case is different. Before their existence can be determined, there is evidence of constitutional disturbance. In the one case, the local symptoms precede the constitutional: in the other, the constitutional precede the local. Which first show themselves in rheumatic fever?

There is much variety in the mode of onset of this disease. Sometimes the initial symptom is a distinct rigor, followed by general febrile disturbance, and the speedy development of the characteristic joint affection. At others, the patient complains at first only of chilliness and general *malaise,* accompanied by aching of limbs. Soon fever is decided, and the pains are localized in the joints. In milder and subacute attacks, the local joint affection is often the first and only thing complained of; but careful inquiry nearly always elicits the fact that the patient had been "out of sorts," or had "had cold" for some days before the joint affection declared itself. In whatever way the disease commences—suddenly by a distinct rigor, or so gradually that the exact time of its onset can scarcely be determined—the local inflammation is preceded by constitutional disturbance.

In rheumatic fever, then, the constitutional disturbance precedes the local inflammation of the joints, and cannot be regarded as altogether consequent on, or symptomatic of, it.

But though this is true, it is equally the case that the full development of the fever is contemporaneous with the height of the joint affection. When once the disease is fully established, the local inflammation and the constitutional disturbance go hand in hand—they rise and fall *pari passu,*—and there can be no question that the febrile disturbance, though antecedent to, is much increased by the local inflammation.

In this respect the joint inflammation of rheumatic fever resembles the local lesions of the eruptive fevers, more than it does common inflammation due to a local cause.

How is the inflammation of the fibrous and serous tissues induced? That it results from the action of the rheumatic miasm there can be no doubt. The question is, "How does the miasm act?"

It may act in one of two ways: either as a direct irritant to these tissues, causing in them the same kind of excitation that cantharides produces in the bladder, and arsenic in the stomach and rectum; or it may act after the manner of a contagium, and owe its action on the fibrous and serous tissues to its propagation in them.

We have already seen that the mode of onset, and general as well as local symptoms of acute rheumatism, are such as can be explained only on the view that its poison is reproduced in the system during the course of the disease. The gradual onset of the rheumatic inflammation, its shifting character, its uncertain course, its occasionally prolonged duration, and its gradual decline, can be explained only on the view that the poison is reproduced in the system during the course of the malady, and that a fresh supply of poison is thus being constantly brought into play. On this view, the occurrence of the local inflammatory lesion is readily explained.

If such be the mode of action of the rheumatic poison—if it owe its morbific effects to its reproduction within the system—the characteristic inflammation of the fibrous and serous tissues will bear, to rheumatic fever, the same relation that the local lesions of the eruptive fevers bear to these diseases. In other words, the seat of the rheumatic inflammation is, on this view, the nidus of the parasitic organism which produces the disease.

The action which takes place in the nidus, is that which implies the fecundation and propagation of the organism, as distinguished from its organic growth. What does such a special action imply? In the absence of any definite knowledge on the subject, it would be natural to suppose that the fecundation of an ovum or seed required a greater expenditure of force than the mere maintenance of its vitality—that a greater degree of energy was required to start those forces which the existence of life implies, than was requisite to keep them up after they had been set agoing. And we know from observation that such is the

case. The immediate consequence of the fecundation of the ovum of one of the higher animals, is an increased flow of blood to it, and increased vascular excitement of the maternal organs concerned in the process. During the period of germination and flowering of many plants, the increased action which accompanies the process may be so great as to cause a decided rise of the temperature of the part in which the action occurs. So great is this rise in some cases, especially in some of the araceæ, that the heat produced may be felt by the naked hand.

"Now, I do not for a moment mean to say that the process which takes place during the fecundation of organized poisons, is the same as that which occurs in the impregnation of ova, and in the germination of seeds. I merely say that it bears to it sufficient analogy to warrant us in founding an argument thereon. Contact with its special nidus, is as essential to the development of the germ of a parasite, as is contact with the seed of the male to the ova of the higher animals, or contact with the pollen to the pistils of plants.

"The contagia, as parasites, find in their nidus something which is essential to their fecundation, and without which they cannot be reproduced. The poison of any of the eruptive fevers may be introduced into the system, but unless it reach its second factor in its nidus, it is not propagated.

"There certainly takes place in the nidus an action which takes place nowhere else, and which must be accompanied by some evolution of force. From what is observed in the case of higher organisms, we may conclude that this evolution of force must be accompanied by increased activity in, and increased vascularity of, the part in which the action occurs. Increased vascularity is the primary and essential condition of the local lesion of each of the eruptive fevers. The part so affected we regard as the nidus in which the contagium finds its second factor; and the localized active hyperæmia which constitutes the local lesion, we regard as the necessary result of the action which accompanies the fecundation of the contagium particles. Active hyperæmia implies hyperaction. Such hyperaction as the fecundation of thousands, or even millions, of germs implies, is adequate to produce the hyperæmia, and even the marked inflammatory mischief, which constitutes the local lesion." (Maclagan, op. cit., p. 181.)

What is here said regarding the eruptive fevers, equally applies to

rheumatic fever. The poison of that disease finds its nidus in the fibrous tissues of the motor apparatus of the body. The inflammation of these tissues, which constitutes the essential and characteristic feature of rheumatic fever, is the necessary accompaniment of the hyperaction which the fecundation of an organism in them implies. The joint inflammation of rheumatic fever, thus bears to the general febrile disturbance of that disease, the same relation that the local lesions of the eruptive fevers bear to their general symptoms.

Just as in the eruptive fevers we find the distribution of this nidus vary both in situation and in extent, so also do we find similar variations in rheumatic fever. In scarlatina the skin and throat are the common seats of the second factor; but it is not always equally distributed between the two. When in excess in the skin, there is an abundant eruption and little sore throat; when in excess in the throat, there is bad sore throat and little or no eruption. So in measles, the second factor has two seats, the skin and the mucous membrane of the respiratory tract. If concentrated in the former, there will be an abundant eruption, and no chest complications; if in the latter, the eruption will be scanty, and the chest complications serious.

It is the same in rheumatic fever; the second factor may be widely distributed over all the serous and fibrous tissues of the motor apparatus; or it may exist only in those of one or two joints, say the knees and ankles. In each case the severity of the attack will be directly as the amount of the second factor. In the former, its wide distribution will lead to a correspondingly extensive local lesion; the heart and all the large joints may be inflamed, and the illness be a severe one. In the latter, the attack will be mild, and the local inflammation confined to the knees and ankles.

The heart complications of acute rheumatism bear to that disease the same relation that throat complications bear to scarlatina, and chest complications to measles. Though by no means a necessary part of the disease, they are normal to, and symptomatic of, it. The cases in which they occur are those in which the rheumatic poison finds its second factor in the vasculo-motor, as well as in the loco-motor, system. Exceptional cases there are, too, in which this second factor exists only in the vasculo-motor system; and in which, therefore, the rheumatic poison manifests its action only on the heart. Such cases are the analo-

gies of those rare instances in which the poisons of the eruptive fevers produce febrile disturbance without the usual eruption. We may have a rheumatic affection of the heart, without contemporaneous joint affection, just as we may have scarlatinal sore throat without other evidence of the disease, and just as we may have typhus sine eruptione, morbilli sine morbillis, and variola sine variolis.

2. *The local inflammation is limited almost entirely to such fibrous and serous textures as are habitually subjected to strain and active movement.*

A highly developed joint, such as suffers in rheumatism, consists of a sac of synovial membrane investing the cartilaginous ends of the bones, and reflected over the fibrous capsule and ligaments. External to this purely articular arrangement are the tendons of the muscles which move the joint, and without which the joint structures proper would be useless. Many of these tendons run in grooves or sheaths, having a lubricating surface similar to that which exists in the joint.

All the structures here enumerated are necessary to the formation and functional completeness of a freely mobile joint. But they do not all suffer when that joint is the seat of rheumatic inflammation. It is only the fibrous and serous textures—the ligaments, tendons, and the lining membranes of the joints and tendinous sheaths—on which the action of the rheumatic poison is habitually exercised.

But when we come to examine the subject more minutely, we find that the serous membranes very often escape, and that the only structures which invariably suffer, are those fibrous textures which are subject to habitual strain.

The symptoms of rheumatic inflammation of a joint are pain, swelling, and redness. Of these, pain is the only one which is invariably present. It is the earliest and most essential symptom of rheumatic disturbance of a joint; without it rheumatism cannot be said to exist. But rheumatic disturbance of a joint frequently occurs without any swelling or redness. In chronic rheumatism, and in mild attacks of the subacute form of the disease, there is seldom any swelling, and never any redness; there is, in short, nothing in the external appearance of the joint by which the existence of the ailment could be diagnosed; there exists only the subjective symptom of pain.

Pain exists in every case of rheumatism of the loco-motor appara-

tus, and is *the* essential symptom of the disease. It depends on, and is the evidence of, inflammation of the fibrous textures. Such inflammation is the primary and essential feature of rheumatism.

Swelling is frequent, but exists only in acute and subacute attacks—that is, in the severer forms of the malady. It is a result of inflammation of, and consequent effusion into, the sac of the synovial membrane. Inflammation of that membrane is not an essential feature of rheumatism. It occurs in all acute, and most subacute attacks, but not in the mild and more chronic forms of the disease. In other words, it occurs only in cases in which the inflammation of the fibrous textures is marked; but not in those in which these textures are only slightly inflamed. Cases in which the joints swell are attended with more pain—the evidence of inflammation of the fibrous textures—than those in which there is no swelling. The greater pain is not due to the synovial inflammation and effusion; for it is severe before there is evidence of the synovial membrane being involved. When we contrast the agony of acute rheumatic inflammation of a joint, with the less severe pain of a more decided synovitis resulting from injury, we get an idea of how much of the pain of the former is due to inflammation of the fibrous textures, and how little of it to inflammation of the synovial membrane.

Swelling is always secondary to pain. Even in the most acute cases, in which the swelling is greatest, and comes on soonest, pain exists for a time before the joint begins to swell. We know, from what is observed in injuries to joints, that inflammation of the synovial membrane very quickly gives rise to effusion and swelling.

Redness of the surface occurs only in cases in which the inflammation is sufficiently severe to lead to the extension of the hyperæmia to the vessels of the skin. In many cases this symptom does not exist. The joints may be very painful and considerably swollen without being red. A slighter amount of inflammation is necessary to its production in joints situated near the surface, such as the wrist and knee, than in those which are more thickly covered, such as the hip and shoulder. In subacute attacks of rheumatism involving several joints, the wrist is often the only one which shows any redness of the surface. This is no doubt due to the fact that in that joint many of the fibrous and tendinous structures are situate almost immediately under the skin. The hyperæmia which accompanies this inflammation is more likely, therefore, to extend to the surface.

What is the meaning of these facts? What their bearing on the pathology of the joint affection?

We find that the fibrous textures are inflamed in *every* case of rheumatism; but that the serous tissues suffer only in those in which the inflammation of the fibrous textures is accompanied by decided febrile disturbance, and is sufficiently marked to render the case more or less acute. We further find that in no case—not even the most acute—is inflammation of the serous textures ever primary: there is always, and in all cases, a period at the commencement of the disease in which the inflammation is confined to the fibrous textures and in which pain is the only local symptom; and only after these textures have been inflamed for at least some hours, is there evidence of inflammation of the synovial membrane.

As the inflammation always commences in the fibrous textures, and as it is only in cases in which the inflammation of these textures is more or less acute, that the synovial membrane suffers, the question naturally presents itself to our minds, whether the inflammation of the synovial lining may not result from the direct extension to that membrane of a prior inflammation of the fibrous ligaments and tendons. In other words, a careful consideration of the facts with which we have to deal, raises a grave doubt whether the rheumatic poison has any direct action on the serous tissues, and whether the inflammation which undoubtedly takes place in them may not be due to the extension of the inflammatory process to them from the contiguous fibrous textures, rather than to any direct action on them of that poison.

The evidence favors the view that such is the case, and that the fibrous structures of the joints are the primary seat of rheumatism. We know that synovial membrane is very susceptible to inflammatory action, and that such action is very liable to spread to it from contiguous structures. Injury to any one point of such a membrane is very apt to be quickly followed by a general inflammation of its whole surface. We know, too, that such inflammation is developed very rapidly, and is speedily followed by effusion into the joint.

Recognizing this peculiarity of synovial membrane, we cannot fail to see that acute inflammation of the fibrous structures over which it is reflected, and with which it is in immediate contact, is very likely to extend from them to it. The more acute the inflammation, the more likely is this to happen.

This is quite in accordance with what is observed in the joint inflammation of rheumatism. It is in acute cases that the synovial membrane is most affected, and that the joint swelling is most marked. It is in such cases that the inflammation of the fibrous textures is most severe, and most liable to spread to surrounding textures.

We shall by-and-by see reason to believe that inflammation of the lining and investing membranes of the heart, is also secondary to prior inflammation of the subjacent fibrous textures of that organ.

3. *The action of the rheumatic poison is confined almost entirely to those of a particular age.*

The age of liability to rheumatic fever is from fifteen to fifty.

This immunity of the very young and very old, can be accounted for only in one or two ways: either the rheumatic poison does not enter their systems; or, having entered, it does not act.

The former is a position which cannot be maintained. There is no reason why an agency which may gain entrance to the system at twenty or fifty years of age, may not equally gain entrance at ten or sixty. The portals of the system are as free and as open at the one age as at the other.

The second is a position which may reasonably be maintained: for there is distinct evidence that some poisons, to which that of rheumatism bears analogy, may, under certain circumstances, be introduced into the system without producing effect. We know, for instance, that a person who has not been vaccinated, and has not had small-pox, cannot be exposed to the poison of that disease without almost certainly taking it. But we also know that, having once suffered, he may be constantly exposed, and may even have the poison directly introduced into his system, without again suffering from its action. So with each of the eruptive fevers—one attack confers, as a rule, immunity from the future action of its poison. Here we have adequate proof that a poison, and a very potent one too, may gain entrance to the system without producing any effect on it. The circumstances which give rise to this immunity we have already referred to. We now note the fact in connection with the acknowledged immunity from rheumatic fever of the young and old, and in exemplication of the view that such immunity is due, not to absence of the rheumatic poison, but to insusceptibility to its action.

We have seen that the rheumatic poison acts almost solely on those fibrous and serous tissues which enjoy a high degree of functional activity, and are subject to a great amount of movement and strain. But these tissues are not equally active at all periods of life. In infancy and early life, the child has not the physical strength and stamina necessary for active movement, and there is no strain thrown on his fibrous tissues. After the age of fourteen or fifteen, matters change. The child has now reached an age at which work and vigorous exercise begin to form part of his daily life; and when adult life is reached, hard work and active exercise are of constant occurrence. This implies vigorous and free movements of the larger joints, and increased force and activity of the heart's action. It necessitates, also, a state of preparedness for such action. At any time he may be called upon to make efforts necessitating such movement and action; and the requisite facilitating and restraining forces must be there to prevent mishap. The period of life at which efforts implying strain on the fibrous textures are made, is from fifteen to fifty, or thereabouts. This, therefore, represents the period of highest functional activity of those serous and fibrous tissues whose function it is to facilitate and restrain movement. It also represents the period of greatest liability to the action of the rheumatic poison.

The period of liability to the action of the rheumatic poison is the period of functional activity of the tissues specially involved in that disease. And in the fact that from fifteen to fifty is the period of such activity, we have the explanation of the special tendency of rheumatic fever to affect people of that age.

The same thing is noted in connection with some of the eruptive fevers. It is specially marked in the case of typhoid. The intestinal glands whose inflammation constitutes the characteristic feature of that disease, exist in infancy in but a rudimentary state. After two or three years, they begin to increase in size and functional activity, and go on increasing till adult life is reached. From that time till middle age they are prominent objects in the intestinal wall. They then begin to diminish in size and functional activity, and go on diminishing as age advances, till in old age they are practically non-existent, and have ceased to exercise any function. The liability to the action of the typhoid poison, is directly as the size and functional activity of these

glands. In infancy and old age the disease is all but unknown. The period of greatest liability to it is from fifteen to thirty-five. All this is inadequately explained on the view that these glands are the nidus in which the typhoid poison finds the second factor necessary to its propagation.

On exactly the same view is to be explained the special tendency of the rheumatic poison to affect people between the ages of fifteen and fifty. This is the period of functional activity of those tissues whose inflammation constitutes the local lesion of the disease, and which bear to the rheumatic poison the same relation that the intestinal glands bear to that of typhoid fever. These tissues form a suitable nidus for the propagation of the rheumatic poison only during their period of functional activity. Before and after this period, they do not present to that poison the conditions requisite to its development and action. Hence, before and after that period, there is insusceptibility to the action of the rheumatic poison.

4. *Hereditary transmission.*

Many diseases are said to run in families—to be transmitted from father to son. And the facts warrant the statement. A gouty parentage gives a liability to gout. The children of phthisical parents are in turn apt to die of the same disease. Rheumatism is also thus inherited.

But when we say that a man inherits a disease from his father, we do not mean to say that he comes into the world suffering from it, or with its seeds already in him. In the case of gout, he may enjoy perfect immunity from it during the greater part of his life, and begin to suffer only when forty or fifty years of age. In the case of phthisis, perfect health may be enjoyed for twenty years, and then the fatal inheritance declare itself. In the case of rheumatism, this inheritance seldom declares itself before fifteen, and is generally lost again after fifty.

The son may be born before the father has himself suffered from the malady which he is believed to have transmitted to his offspring. Or the father may even not suffer at all: he may be simply the medium of transmission to his son of a malady from which his forefathers had suffered. Evidently it is not the disease itself, but only the family tendency to it, which is transmitted. To transmit an actual disease, the father must have its poison in his system when his son is begotten; in which case the child will be born with the malady already developed.

This is well instanced in the case of syphilis. But that is a very different thing from what occurs in the case of rheumatism. What is there transmitted, is not the disease, but a tendency to it—a greater or less liability to contract it.

This tendency is generally referred to as a constitutional predisposition. But to give it a name is to indicate, not to explain, its existence. What is a constitutional predisposition to rheumatism? Wherein does it consist? And what do we mean when we say that a man has inherited rheumatism from his father?

Acute rheumatism consists in inflammation of the white fibrous and serous tissues of the motor apparatus. Its poison is a miasmatic organism, which is propagated in the system, and finds the nidus requisite to this propagation, in those tissues whose inflammation constitutes the specific lesion of the disease. For the production of acute rheumatism, therefore, two factors are necessary—first, the poison introduced from without; second, that peculiar condition of the tissues of the motor apparatus which imparts to them their special fitness to act as a nidus for this poison. Which of these factors is it that is transmitted? or is it both? One or both it must be, if we recognize transmission at all.

It is certainly not both, for their co-existence in the system at birth would give rise to the disease in the infant. As certainly it is not the first, for a miasmatic poison is essentially one which is received into the system from without, and which gives rise to a disease which is not communicable. It can only be the second: it can only be that peculiar condition of the tissues of the motor apparatus which renders them a fitting nidus for the propagation of the rheumatic poison.

The difference between a rheumatic and a non-rheumatic subject is, that the motor apparatus of the former contains that special ingredient which is requisite to the propagation and action of the rheumatic poison; while that of the latter does not. Between the fibrous tissues of the two men there is no difference that can be detected either by the anatomist or the chemist; but in the one, these tissues afford a nidus for the propagation of the rheumatic poison—in the other, they do not. In the one the tissues of the motor apparatus contain something which is wanting in those of the other. It is the presence of this something, which constitutes the peculiarity of the rheumatic constitution. It is the tendency to the development of this peculiarity, which is trans-

mitted from father to son, and makes each generation susceptible to the action of the rheumatic poison.

That such a peculiarity should be inherited, consists with all that we know of hereditary transmission. There is no reason why internal peculiarities should not be transmitted, as well as external—why a peculiar condition of the brain, of the stomach, of the liver, should not be handed down from father to son, as well as a special cast of features, a particular color of hair, or a peculiar shape of the limbs. And we know as a fact that certain peculiarities of internal organs are transmitted.

Furthermore, there is no reason why peculiarities of individual structures should not descend from generation to generation, as well as peculiarities of individual organs: indeed, peculiarity of an entire organ presupposes peculiarity of its individual parts.

It consists with all reason, that peculiarities of the motor system should be inherited, as well as peculiarities of the nervous, digestive, osseous, and other systems of the body.

That some peculiar condition of the motor system is handed down in rheumatism, we know. That this condition declares itself by a special susceptibility of the tissues of the motor apparatus to the action of the rheumatic poison, we also know.

But more than this we cannot say; for in this, as in all other cases of hereditary transmission, we can only indicate, not explain, the fact. So far as the bearing of this fact on the miasmatic theory of rheumatism is concerned, we can only say that that theory perfectly consists with it.

5. *The presence in the blood of an excess of fibrine.*

In many forms of inflammation, the blood contains an increased quantity of fibrine. In acute rheumatism this excess is specially marked.

Fibrine was at one time believed to be an important nutrient constituent of the blood. It is now known that such is not the case. There is ample evidence that it is a product of tissue waste—an excrementitious, rather than a nutrient, compound. The evidence of this is, that it accumulates during fasting, and during many ailments accompanied by increased waste. It exists also in increased quantity in the blood after fatiguing exercise; and Brown-Sequard has shown that

the more a muscle is exercised by galvanism, the more fibrine does the blood issuing from it contain. There can be no reasonable doubt that fibrine is a product of the retrograde metamorphosis of nitrogenous tissue.

We know that inflammation causes increased metamorphosis of the tissue in which it occurs. We know that rheumatism consists in inflammation of the tissues of the motor apparatus. We know that these tissues are the chief source of the fibrine of the blood. We know, therefore, that rheumatic inflammation must be accompanied by increased formation of fibrine. The presence in the blood of an excess of fibrine during the course of acute rheumatism, is thus a necessary result of the morbid action which constitutes the characteristic feature of the disease. It results from increased metamorphosis of the nitrogenous elements of muscle and fibrous tissue.

6. *The presence in the blood of an excess of lactic acid.*

This, one of the most characteristic phenomena of acute rheumatism, has already been considered.

It has been shown that lactic acid is a normal product of the retrograde metamorphosis of muscular tissue; that its formation in excess during muscular exercise results from increased wear and tear of the tissues of the motor apparatus; and that its excessive formation in acute rheumatism is due to the same cause, only differently induced. In the one case, the increased metamorphosis results from exaltation of a natural function; in the other, it is a consequence of a pathological process, viz., inflammation of the tissues of the motor apparatus, induced by the action of the rheumatic poison, and leading to excessive formation of lactic acid, in the manner already explained.

The argument may be briefly summed up as follows:—

Rheumatism is essentially a disease of the motor apparatus of the body. Acute rheumatism essentially consists in acute inflammation of the parts of that apparatus which are most subject to strain. The tissues chiefly involved are the white fibrous. But these are so intimately and inseparably connected both anatomically and physiologically with the muscles, that vascular disturbance of the one cannot fail to be participated in by the other. The inflammation of the fibrous textures which constitutes the local lesion of acute rheumatism, must therefore be accompanied by increased metamorphosis of the highly vascular

muscles which, with them, form the motor apparatus of the affected joints. As a result of the action of the rheumatic poison, we thus have increased retrograde metamorphosis of the whole motor apparatus, muscular as well as fibrous. Fibrous tissue contains only nitrogenous material; muscular tissue contains both nitrogenous and non-nitrogenous. Its non-nitrogenous material is glucose. We know that glucose is the natural source of lactic acid in health. It is almost certainly also its source in disease.

The difficulty has been to account for the increased metamorphosis of the glucose. On the view which has been advanced as to the nature of the rheumatic process, this difficulty is satisfactorily disposed of.

According to the miasmatic theory, the increased formation of lactic acid in acute rheumatism, results from increased metamorphosis of glucose, the *non-nitrogenous* element of the tissues of the motor apparatus, just as increased formation of fibrine and of urea result from increased metamorphosis of the *nitrogenous* elements of the same tissues. Each is a necessary result of the action of the rheumatic poison on the tissues of the motor apparatus.

To another possible source of lactic acid in acute rheumatism a brief reference must be made.

The rheumatic poison is introduced from without, is reproduced in the system, but is not eliminated in an active form. What, then, becomes of it? It must be destroyed in the system. In the absence of any definite knowledge of the composition of the poison, we do not know the exact nature of the changes which such an event would imply. There is, however, nothing in the nature and composition of an organism, such as we believe the rheumatic poison to be, and nothing in the nature and composition of lactic acid, to prevent us from regarding the latter as a possible product of the destructive disintegration of the former. The first decided evidence of an excess of lactic acid is its excretion by the skin. By the time that this occurs, the rheumatic poison has produced other symptoms characteristic of its action. It has been reproduced, and is undergoing disintegration as well as reproduction. Lactic acid is a possible product of such disintegration. Its presence in excess might, therefore, result from the destructive disintegration of the organism which produces the rheumatism.

Whichever view we take—whether we regard the excessive formation of lactic acid as a result of increased disintegration of muscle, as a result of the destructive disintegration of the rheumatic poison, or as a result of both processes,—it is evident that we must look upon the acid as one of the results of the action of the rheumatic poison and in no case as in itself constituting that poison.

The view that the acid is a consequence of increased metamorphosis of muscular tissue, is clearly that which most commends itself to our reason. The other is a mere supposition, to which it is right that a reference should be made, but which has little to commend itself to us. It consists with either view that the more acute the case—that is, the greater the reproduction of the rheumatic poison—the larger the quantity of lactic acid formed.

7. *The occurrence of profuse perspirations.*

Abnormally free action of the skin is a characteristic of acute rheumatism. As a rule, the more acute the case, and the more intense the joint inflammation, the more free is this action. The perspiration has an acid reaction, and continues during the whole course of the acute symptoms.

By some these sweats have been regarded as exhausting and debilitating, and, therefore, as injurious. By others they have been looked upon as salutary. When two such antagonistic opinions are held, we may safely infer that neither expresses the whole truth.

In some circumstances, profuse perspiration is both evidence of weakness, and a cause of increasing debility. In others, it is unquestionably salutary, and seems to be the means by which certain disturbances of the system are brought to an end. In rheumatic fever it cannot be said to have either effect.

There is no evidence that it causes such debility as results from the night sweats of phthisis; but those who study it in connection with these sweats, will naturally conclude that it is weakening. There is no evidence that it produces the salutary effects which are noted in connection with the critical perspirations of pneumonia, and other acute febrile ailments; but those who study it in connection with these critical sweats, will naturally conclude that it is salutary.

All cases of phthisis do not have night sweats: they are among the unfavorable symptoms of some cases.

All cases of pneumonia do not have a critical perspiration: it is one of the favorable symptoms of some cases.

But all cases of acute rheumatism have acid sweats; and have them, not at one period only, but continuously through the whole course of the fully developed disease.

There is no evidence that they exercise a favorable influence on the course of the ailment: there is no evidence that they influence it unfavorably. The acid sweats of acute rheumatism are altogether peculiar—altogether different from those noted in connection with exhausting maladies, and the crisis of acute febrile ailments. They constitute one of the ordinary characteristics of the disease—one of the common results of the action of the rheumatic poison. How are they produced?

We have seen that the blood in acute rheumatism contains an excess of lactic acid. This it is which gives to the perspiration its acid reaction and odor. As this acid has been regarded by many as the cause of the rheumatism, its excretion by the skin has naturally been looked upon as a thing to be desired; and this is the foundation for the belief that the profuse perspiration of acute rheumatism is salutary. For so, on this view of the matter, it ought to be. The probability is a hypothetical one, however, which is not supported by fact; for practically we find that the most profuse perspiration affords no relief to the pain. In fact the pain is, as a rule, most severe in cases in which the sweating is most free.

When considering the lactic acid theory we saw that one of the most common and constant effects of the internal administration of that acid, was increased action of the skin. The dry and branny skin of cases of diabetes becomes, under its influence, moist and perspiring. If such be the effect of a comparatively small quantity given by the mouth, in a disease in which there is great difficulty in getting the skin to act at all, what is likely to be the effect of its formation in large quantity in the system during the course of a malady in which there is no difficulty in getting the skin to act? Clearly profuse perspiration. That lactic acid is formed in very large quantity in the course of acute rheumatism, is evidenced by the quantity eliminated by the skin. Normally it is converted in the system into carbonic acid and water, and in that form

is thrown off by the lungs and skin. The elimination of the unchanged acid indicates that there has been formed a larger quantity that can be so converted.

There can be no reasonable doubt that the acid perspirations of acute rheumatism are due, not to an effort of nature to eliminate the rheumatic poison, but to the stimulant action on the skin of the excess of lactic acid formed during the increased metamorphosis of the tissues of the motor apparatus. These perspirations are to be regarded as neither prejudical nor beneficial; but as simply one of the necessary symptoms of the disease during whose course they occur. They occupy in its symptomatology the same position as increased elimination of urea, and bear to the local lesion of rheumatic fever the same relation. The excess of acid is the result of increased metamorphosis of the non-nitrogenous, the excess of urea the result of increased metamorphosis of the nitrogenous, elements of muscle.

8. *The shifting character of the joint affection.*

This is one of the most striking peculiarities of a rheumatic attack. In the history of all forms of the disease, acute, subacute, and chronic, it occupies a prominent place; and no theory of rheumatism can be regarded as satisfactory, which does not recognize and account for it.

It is impossible to explain it on any theory which recognizes only the existence of a poison equally distributed through the blood, acting like an ordinary medicinal or poisonous agency, and acting, therefore, equally and continuously so long as it exists in adequate quantity.

The miasmatic theory, which regards the rheumatic poison as a parasitic organism, requiring for its development and action a second factor which is localized in fibrous and serous tissues, which exists in varying amount in different parts of these tissues, and which may be exhausted and renewed over and over again, satisfactorily explains this, as all the other peculiarities of the local lesion of acute rheumatism.

The second factor may exist in larger quantity in one joint than in another. In that which contains most of it, the inflammation will be most marked and of longest duration. But the second factor may be exhausted and renewed again. Its exhaustion implies decline of inflammation, its renewal a re-accession of it. The tendency to its renewal may be so great that it may take place in the fibrous textures of

a given joint more than once during the course of a single attack of the disease. Such a joint would, therefore, suffer more than once. What applies to one joint, applies to all.

The exhaustion of the second factor in one joint, may coincide in point of time with its renewal in another. In that case the decline of the inflammation in the former, will coincide with its onset in the latter. In this we have the explanation of the apparent occurrence of metastasis. The inflammation seems to leave one joint and go to another; in reality it is a mere coincidence. The decline of the inflammation in the one, has nothing to do with its appearance in the other; by mere accident the second factor is exhausted in the one, at the same time that it is renewed in the other. And it would be wonderful indeed if such a coincidence did not sometimes occur. Occasionally the metastasis seems to be to the heart: but here, too, it is a mere coincidence; for, in its tendency to become the seat of rheumatic inflammation, the heart is in exactly the same position as a joint.

During the course of even the most continuous and prolonged attack of acute rheumatism there are noted from time to time partial remissions, and subsequent exacerbations, both of fever and of pain. The fever is not a continued one; and the joints first affected do not suffer continuously, and with equal severity, during the whole course of the attack. There are many ups and downs, and shiftings and changes, in the course of both the general disturbance and the local inflammation, before the time is reached at which both begin permanently to decline. During the course of the attack, all the large joints of the body may suffer, but seldom, if ever, all at the same time, or all in the same degree.

As already stated, such prolonged acute attacks are to be regarded as a succession of short ones, which follow each other so closely, that the one overlaps and runs into the other. There is no distinct interval to separate them from each other, but only a partial remission to mark their individual existence. This view quite explains the shifting character of the joint affection.

Another peculiarity of rheumatic inflammation may here be referred to. It tends to affect the same joints on both sides of the body. If one knee or elbow is inflamed, the probability is that the other will also suffer: if the right wrist is affected, the left is not unlikely to be involved, either at the same time, or shortly afterwards.

Of this peculiarity the miasmatic theory affords a reasonable explanation. That which determines the seat of the action of the rheumatic poison, is the presence of the second factor, the irregular and uncertain distribution of which has already been referred to. If this factor exist only in the fibrous textures of the knees and ankles, only the knees and ankles will afford a suitable nidus to the rheumatic poison, and only the knees and ankles will become inflamed during its action. So with all the other joints: they are, or they are not affected during a rheumatic attack, according as their fibrous textures are, or are not, a suitable nidus for the rheumatic poison. If the second factor, whose presence makes the fibrous textures of a joint a suitable nidus, exist in those of the right wrist, the probability is that if it exist anywhere else it will be in the left wrist: the same individual peculiarity which led to its existence in a given joint of one side, leading also to its development in the corresponding joint of the other.

Hitherto we have dealt with the action of the rheumatic poison on the *loco-motor* apparatus. We pass now to the consideration of its action on the *vasculo-motor*.

CHAPTER XI.

RHEUMATISM OF THE VASCULO-MOTOR APPARATUS.

The vasculo-motor apparatus is made up of the following textures:—

1. The hollow muscular substance of the heart, which, by its contraction, initiates the movement of the blood.

2. Rings of white fibrous tissue, which surround and form the basis of the arterial and arieulo-ventricular openings; and to which the muscular fibres are attached.

3. Fibrinous valves whose structure is continuous with that of the rings, and whose function it is to close the various openings of the heart, and keep the circulating fluid in the proper channel.

4. A membrane which lines the interior of the heart's cavities, and is reflected over the fibrous structure of the valves; and whose smooth surface facilitates the onward flow of the blood.

5. An investing membrane which covers the heart externally, and whose peculiar formation and smooth, glistening surface facilitate the free action of that organ.

All these structures, except the endocardium, find their analogues in those which go to form a complete and perfect joint.

The function of cardiac muscle, like that of voluntary muscle, is to initiate movement.

The function of the fibrous structure of the rings and valves, like that of the fibrous tendons and ligaments, is to afford attachment to muscle, to regulate normal, and to resist abnormal, movement.

The function of the pericardium, like that of the synovial membrane of the joints, is to facilitate free movement.

The endocardium alone has no analogue in the loco-motor apparatus.

When considering the action of the rheumatic poison on that apparatus, we saw that the structures on which it acts primarily and chiefly, are those fibrous textures which are habitually the seat of strain, the ligaments and tendons.

It is the same in the vasculo-motor apparatus. The parts which

suffer most, are the fibrous rings and valves—the structures, that is, whose function is essentially one of resistance—the former in consequence of the attachment to them of the muscular fibres; the latter in consequence of the pressure of the blood column.

It is its tendency to affect the heart that imparts to rheumatism its most serious features. In the majority of fatal cases, death is attributable to some form of cardiac inflammation.

Bouillaud was the first who insisted on the essential nature of the connection between rheumatism and this inflammation. Its frequent occurrence in the course of that disease had indeed been pointed out by others before him, notably by Pringle.[1] But it is to this distinguished French physician that we must accord the credit of having first insisted on the frequency, and true nature, of the heart affection. Before his time it was looked upon as a sort of metastasis, or retrocession of the inflammation from the joints to the heart. He regarded it as "one of the elements of the disease;" and as early as 1835 advocated the view, which has since been generally accepted, that pericarditis and endocarditis are of frequent occurrence in the course of acute rheumatism, and are to be regarded as produced in the same way as the joint inflammation.

"La péricardite existe chez la moitié environ des individus affectés d'un violent rhumatisme articulaire aigu. Sous ce point de vue la péricardite n'est, en quelque sort, qu'un des éléments de la maladie dite rhumatisme articulaire aigu, laquelle, considerée d'une manière plus large et plus exacte qu'on ne l'a fait jusqu'ici, constitute une inflammation de tous les tissus séro-fibreux en général, développée sous une influence spéciale. Or, le péricarde étant de nature séro-fibreuse, comme le tissu où reside le rhumatisme articulaire proprement dit, il n'est pas étonnant que la péricardite cöincide si souvent avec ce dernier: que le rhumatisme du péricarde, en un mot, ait lieu dans les circonstances qui produisent un rhumatisme des synoviales articulaires et des tissus fibreux sur lesquels elles se déploient, lequel n'est, pour ainsi dire, qu'une péricardite articulaire.

"L'endocardite, à l'instar de la péricardite, se manifeste sous les mêmes influences que le rhumatisme articulaire aigu: et bien que cette

[1] Observations on Diseases of the Army, by Sir John Pringle. 1761.

phlegmasie puisse éclater quelquefois pendant le cours d'un grand rhumatisme articulaire aigu et d'une manière purement *métastatique*, suivant l'expression de certains pathologistes, il n'en est pas moins vrai que, le plus souvent, le tissu séro-fibreux interne du cœur se prend en même temps que celui des articulations: c'est aussi ce que nous avons vu pour le tissu séro-fibreux externe du cœur. Sous le point de vue de leur structure et de leurs fonctions, les parties du cœur qui s'enflamment par l'influence des causes productrices du rhumatisme articulaire ont la plus grande analogie avec les parties des articulations qui sont le siège de ce dernier. Les cavités du péricarde et de l'endocarde représentant, sous le rapport qui nous occupe, des espèces de cavités articulaires, il n'est pas étonnant que leurs phlegmasies cöexistent si souvent avec celles des cavités articulaires proprement dites."[1]

In all forms of rheumatism, acute, subacute, and chronic, the heart is apt to suffer. In the acute, the cardiac inflammation partakes of the generally acute character of the attack, and the symptoms are well marked from the commencement. In the subacute, the symptoms are less marked, and the immediate result of the cardiac mischief less a source of anxiety. In the chronic, its onset is so gradual that the cardiac affection seldom attracts attention until it is so far advanced as to cause serious disturbance of the heart's action, and the general symptoms of cardiac disease.

The exact proportion of cases of acute and subacute rheumatism during whose course recent cardiac inflammation occurs, is differently stated by different observers. And the nature of the question is such that discrepancies must exist.

In acute attacks, the heart is more apt to suffer than in subacute; and young patients are more liable to this complication than old ones. The acuteness of the attack, and the age of the sufferer, are thus important elements in determining whether or not cardiac complications are likely to occur. An observer, the majority of whose cases are subacute, and the average age of whose patients is thirty, will have a smaller

[1] Traité Clinique des Maladies du Cœur, 1835: and Traité Clinique du Rhumatisme Articulaire, 1840. Par J. Bouillaud, Professeur de Clinique Médicale à la Faculté de Médecine de Paris; Membre de l'Académie Royale de Médecine, etc.

percentage of cardiac complications than one who happens to have a larger number of acute cases, and the average age of whose patients is twen

Fuller and others have endeavored, in studying this question, to distinguish between acute and subacute rheumatism. But independently of the difficulty, nay the impossibility, of drawing a distinct line of demarcation between them, there is no pathological reason for doing so. Acute and subacute rheumatism are merely different degrees of severity of the same disease. That the heart is more apt to suffer in acute cases, is no doubt true; but this may be partly due to the more frequent occurrence of such cases in young people: and we sufficiently express the fact when we say that the more acute the attack, the more likely is the heart to suffer during its course.

A study of the statistics bearing on this point, leads to the conclusion that we are very near the truth when we say that, in the course of acute and subacute rheumatism, recent cardiac inflammation occurs in about thirty per cent., or in nearly one case in three. But such a general statement of the fact, is bald and misleading, without the additional statement that, as years advance, the tendency to such complications diminishes.

Here we are brought face to face with two facts which are specially prominent in the history of cardiac rheumatism:—

1. Rheumatic inflammation of the heart is most common in young people.

2. It is more apt to occur in the acute than the subacute form of the disease.

If the miasmatic theory be correct, it should afford a reasonable explanation of these, as of all the other phenomena of rheumatism.

1. *The heart is specially apt to suffer in young people.*

This is a fact which has been observed and commented on by most writers on the subject. One of the most recent of these, Dr. Peacock,[1] gives it as the result of his observations on 233 cases of acute and subacute rheumatism, that of those under twenty-one years of age, 33.3

[1] St. Thomas's Hospital Reports, Vol. VI., 1875; and Vol. X., 1879.

per cent. suffered from recent cardiac disease; while of those over forty, only 16.6 so suffered; "showing that the occurrence of cardiac complication is much more to be apprehended in young people than at more advanced ages." This accords with general experience. What is the explanation of it?

We have seen that rheumatism of the loco-motor apparatus is essentially a disease of adolescence and early manhood; and that the textures which suffer most, are the fibro-serous tissues of the large joints. The general explanation of these facts is, that the tendency of a given portion of fibrous or serous tissue to be affected by the rheumatic poison, is directly as its functional activity. Adolescence and early manhood are the periods of life at which the functional activity of the loco-motor apparatus is at its height. The large joints are the parts of that apparatus which have most work to do. Hence rheumatism is most common in young people, and in the large joints.

Applying the same reasoning to the case of the heart, we find an adequate explanation of the fact which we are now considering—that that organ is more apt to be the seat of recent rheumatic inflammation in young people, than in those of more mature years.

Muscular exertion increases the force and frequency of the heart's action. The more work the loco-motor apparatus is called upon to do, the greater is the demand for blood in its textures, and the greater the force and frequency of the heart's action.

In other words, the loco-motor and the vasculo-motor apparatus work hand in hand; functional activity of the former necessitates functional activity of the latter. In this physiological fact we have the explanation of the pathological one which we are now considering. Rheumatism of the loco-motor apparatus is most common in youth, because youth is the time at which the tissues involved in that disease enjoy the highest degree of functional activity. Rheumatism of the vasculo-motor is most common at the same age, and for the same reason. Sudden and rapid movements, involving correspondingly sudden and rapid increase in the force and frequency of the heart's action, are more frequent before than after the age of forty. Before that age the heart's structures are, therefore, subjected to greater and more frequent strain than they are called upon to bear in more mature

years. With the decreasing functional activity of advancing years, comes also diminished susceptibility to the action of the rheumatic poison.

It is a *clinical* fact that the age of susceptibility to the action of the rheumatic poison is from fifteen to fifty.

It is a *physiological* fact that the tissues on which that poison acts have a higher degree of functional activity during the earlier, than during the later, years of that period.

It is a *pathological* fact that the tendency of a given portion of tissue to be affected by the rheumatic poison is directly as its functional activity.

It follows that the textures of the heart must be more subject to rheumatic inflammation in youth than they are in more mature years. And all observation shows that they are so.

2. *Inflammation of the vasculo-motor apparatus is more common in acute than in subacute attacks of rheumatism.*

What is an acute, and what a subacute, attack?

An *acute* attack is one in which the rheumatic inflammation is both extensive and severe; affecting several joints, and affecting them smartly. In other words, it is a rheumatic attack occurring in one in whom the rheumatic constitution is very marked; in the fibrous tissues of whose motor apparatus the second factor requisite to the action of the rheumatic poison, is abundantly and widely distributed; and on whom, therefore, that poison exercises a very decided action. The more abundant and wide the distribution of the second factor, the more likely is it to exist in the vasculo-motor as well as in the loco-motor apparatus, and the more likely is the heart to be affected.

As a result of its abundance, the inflammation of the individual joints is severe: as a result of its wide distribution, many joints suffer.

We have seen that there are fifteen common seats of rheumatic inflammation—fourteen in the loco-motor, and one in the vasculo-motor system. The wider the distribution of the second factor, the larger the number of these seats likely to suffer at one time. In this respect, the heart is in the same position as a joint; so that the wider and more abundant the distribution of the second factor, the more likely is that organ to suffer.

Thus the same circumstances which make a rheumatic attack acute and sevcre, tend also to give rise to heart complications: and thus is explained the fact that such complications are most apt to occur in acute cases. The heart suffers in such cases for the same reason that a large number of joints do.

A *subacute* attack is one in which the rheumatic inflammation is neither extensive nor severe; affecting few joints, and affecting them in a comparatively mild manner. In other words, it is a rheumatic attack occurring in one in whom the rheumatic constitution is not marked; in the fibrous tissues of whose motor apparatus the second factor requisite to the action of the rheumatic poison, is but sparsely distributed; and on whom, therefore, that poison exercises a comparatively slight action.

The more scanty the quantity, and sparse the distribution, of the second factor, the less severe the inflammation of individual joints, the fewer the number likely to suffer, and the less the likelihood of the heart being affected.

The same circumstance which renders the attack mild, diminishes the tendency to heart complications.

Given a severe and acute rheumatic attack, during whose course ten of the fifteen common rheumatic centres are affected—the heart is more likely to be among the ten which suffer than among the five which escape: the chances are two to one against it. Given a mild and subacute attack, during whose course only five centres are affected—the heart is more likely to be among the ten which escape than among the five which suffer: the chanees are two to one in its favor.

The effect of age in increasing and diminishing the danger to the heart we have already considered.

The influence of these two agencies, the age of the sufferer, and the severity of the attack, ought to be considered conjointly; for severe attacks of acute rheumatism seldom occur except in youth; and nearly, if not quite, always in youth for the first time. It is probable that the severity of the attack has, in the manner just explained, as much to do with the production of the heart affection, as has the youth of the sufferer.

The rheumatie constitution is not acquired, but natural—maybe

inherited. A man who has it, can scarcely reach the age of forty in a temperate climate, without suffering from rheumatism: and he is more likely to suffer for the first time between the ages of twenty and thirty, than between thirty and forty—and that simply because the former decade comes first.

If his constitution be a markedly rheumatic one, he will suffer severely, and the majority of his rheumatic centres will be affected. The heart is more likely to be in the majority which suffer, than in the minority which escape. That organ suffers, therefore, not so much because the man is young, as because his constitution is a markedly rheumatic one; and because exposure to the rheumatic poison is too common to permit of the likelihood of his getting beyond youth without suffering from its action.

That the rheumatic constitution is less marked after middle age, has already been seen. This involves diminished susceptibility to the action of the rheumatic poison: and this is common to the whole motor system —the heart as well as the joints.

Rheumatic inflammation of the heart is generally described as occurring under the three forms of endocarditis, pericarditis, and myocarditis, — inflammation of the lining membrane, inflammation of the investing membrane, and inflammation of the muscular substance.

That each of these different structures is frequently inflamed, there can be no doubt. And yet this classification of the various forms of cardiac inflammation is, from a pathological point of view, inaccurate and misleading. Its fault and its weakness consist in its making no mention of the fibrous structures of the heart. We shall presently see that there is good reason to regard these structures as the chief seat of the action of the rheumatic poison; and to look upon inflammation of the investing membrane as often, and inflammation of the lining membrane as always, secondary to prior inflammation of the subjacent fibrous structures.

But as this classification of the different forms of inflammation about the heart, is simple from an anatomical, and not positively erroneous from a pathological, point of view; and as it, moreover, possesses the advantages pertaining to convenience and long usage, we shall continue

to employ it, rather than try to introduce the complication of a fresh nomenclature. The neglect of the fibrous structures which forms its fault, we shall endeavor to rectify by grouping these structures with the lining membrane, and including under the term endocarditis, not only inflammation of the lining membrane proper, but also inflammation of the fibrous texture of the rings and valves.

CHAPTER XII.

ENDOCARDITIS.

By the endocardium the anatomist means the thin transparent membrane which lines the interior of all the cavities of the heart; is reflected over its valves and muscular folds; is continuous, on the left side, with the lining membranes of the aorta and of the pulmonary veins; and, on the right, with those of the pulmonary artery and systematic veins.

The pathologist must attach to the term a wider meaning, and include under it, all the structures which lie inside the heart—the fibrous rings and valves, as well as the lining membrane.

It is of importance, in connection with our present subject, that this distinction should be borne in mind; for we shall presently see that the endocardium of the anatomist, the lining membrane of the heart properly so called, is probably never the primary seat of rheumatic inflammation.

We now use the term in its wider pathological sense.

By endocarditis we mean inflammation of any or all of the non-muscular structures situated *inside* the heart—the fibrous texture of the rings and valves, as well as the lining membrane.

In the natural history of endocarditis two facts stand out prominently: first, it rarely affects the right side of the heart; second, it is confined to the region of the fibrous rings and valves. It is incumbent upon us to consider and, if possible, explain these two peculiarities.

1. *Endocarditis rarely affects the right side of the heart.*

Rheumatic endocarditis is produced in the same way as rheumatic arthritis, and is due to the operation of the same agency.

In considering the action of the rheumatic poison on the loco-motor apparatus, we saw that the parts of that apparatus which suffer most,

are those which enjoy the highest degree of functional activity, and are habitually subject to free movement and active strain—the large joints. We further saw that the particular structures in these joints which are the seat of rheumatic inflammation, are those on which the strain falls —the fibrous ligaments and tendons.

Applying this to the case of the heart, we find in it a sufficient explanation of the tendency of the rheumatic poison to affect the left, rather than the right, side of that organ. For it is with the vasculo-motor as with the loco-motor apparatus—with the heart as with the joints—the rheumatic poison acts chiefly on the fibrous textures which enjoy the highest degree of functional activity, and are most subject to strain. The valves of the heart consist mainly of white fibrous or tendinous material, similar to that which forms the ligaments of the joints and the tendons of voluntary muscles. Those of the right side have the same structure as those of the left—only they are thinner and contain less of the tendinous material.

They are thinner and weaker because they have much less work to do—much less strain to bear.

The difference between the two sides of the heart in this respect, is evidenced by a reference to the contractile force of each ventricle. The walls of the left ventricle are much stronger and thicker than those of the right, "the proportion between them in this respect being as three to one."[1] It follows from this that the left ventricle acts with three times the force of the right, and that the valve which closes the left auriculo-ventricular orifice is subject to three times the strain which is thrown upon that which closes the corresponding orifice of the right side. "The work done by the right ventricle may be set down as one-third of that of the left."[2]

The fibrous textures of the right side of the heart thus bear to those of the left, the same relation that the fibrous ligaments of the small joints bear to those of the large: they are not subject to the same strain; they have not the same degree of functional activity; and they do not suffer in the same way from the action of the rheumatic poison. The right side of the heart escapes for the same reason that the joints of the toes do.

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[1] Quain's Anatomy. [2] McKendrick's Physiology.

2. *Endocardial inflammation is limited to the fibrous rings and valves.*

Inflammation never affects the whole surface of the lining membrane of the heart. It is almost entirely limited to the part which is reflected over the valves; and when other parts suffer, the mischief is almost invariably attributable to mechanical injury, produced by the rubbing on the affected portion of the endocardial surface, of an already damaged valvular segment. Moreover, the inflammation does not affect the whole valvular surface: only one side of a segment suffers—that, namely, which comes in contact with another segment in the act of closure,—in the aortic valve, its convex surface, and in the mitral, its auricular. The damage is further limited in its early stage to the line at which the segments come into contact. This is well shown in Figs. 1 and 2.

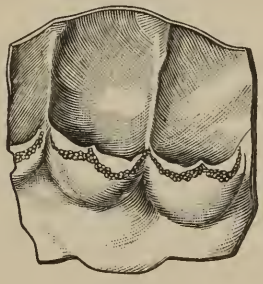

Fig. 1.

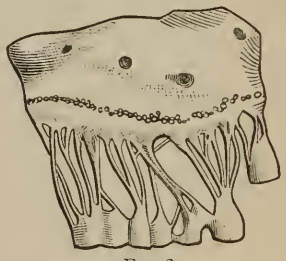

Fig. 2.

Fig. 1.—Inflammation of Aortic Valves.—The earlier stage of the process. Showing the situation of the inflammatory granulations.

Fig. 2.—Inflammation of Mitral Valve.—The earlier stage of process. Valve seen from the auricular surface. Showing the situation of the inflammatory granulations.

The limitation of the disease to this particular part of the valve, has been attributed to the fact that it is the part which is most exposed to friction. "In its earliest stages it always occurs near the edges of a valve in the formation of a line of little elevations along the contact line of its segments, where the friction is greatest."[1]

"It is those portions of the valve which come into contact in the act of closure, and are thus most exposed to friction, which are especially involved, and in which the changes usually commence."[2]

[1] Lectures on Pathological Anatomy, by Samuel Wilks, M.D., F.R.S., and Walter Moxon, M.D., F.R.C.P.

[2] An Introduction to Pathology and Morbid Anatomy, by T. Henry Green, M.D., F.R.C.P.

Of the important part played by friction in the production of inflammation of the lining membrane of the heart, there can be no doubt. Occurring in other than its valvular portion, it is almost always due to the rubbing on its surface of a damaged valve. Knowing this to be the case,—and finding that inflammation of its valvular portion commences at the line of contact of the different segments of the valves, and therefore at the point at which, if anywhere, they are apt to rub,—we cannot fail to see that there is good reason for the belief that friction plays an important part in the production of inflammation of the lining membrane of the heart's cavities.

But the question arises—Why is there friction? Why do the segments of the valves rub against each other? When a valve is already damaged or roughened, it is easy to see how further damage may be done; but in a smooth uninjured valve how is the mischief set agoing? It cannot be that the valves constantly and naturally rub against each other—for in that case, if friction produced endocarditis, no one would be free from it; rheumatic and non-rheumatic subjects would equally suffer; and a smooth healthy valve would be the exception.

For the segments of the valves to come in contact is natural; but contact does not imply friction. Healthy valves normally come into firm and close contact, without in any way rubbing against and irritating each other; and this all the valves of the heart do 70 times every minute—100,800 times every day,—and yet there is no evidence of friction or irritation, until suddenly some day—after this smooth action has gone on uninterruptedly at this rate for maybe twenty-five years, and after the segments of each set of valves have, without injury and without rubbing, come into close and direct contact more than nine hundred millions of times—suddenly some day, the rheumatic poison gains entrance to the system, and the smooth working of the valves comes to an end—they begin to rub; the friction gives rise to irritation and inflammation of the surface of the valve, and the symptoms and signs of endocarditis are developed. How is this? How can the rheumatic poison cause the segments of the valves to rub against and irritate each other? That they do rub is undoubted. That the rheumatic poison is the cause of the morbid change is equally undoubted. The question which we have to consider is how the friction is produced.

If the inflammation of the endocardial covering of the valve be the

result of friction—and there is no reason to doubt that it is so; and if this friction be a result of the action of the rheumatic poison on the valve—and there is no reason to doubt that such is the case,—it is evident that there must be a stage of the valvular lesion which precedes the inflammation of the endocardial covering. If the morbid change which takes place in that covering is produced by friction, there must be some prior change in the valve, interfering with the naturally smooth and innocuous contact of its segments, and causing them to rub against each other; there must, in short, be a stage of the endocardial change which precedes the friction.

Wherein does this stage consist?

Structurally, a valve consists of two folds of the endocardium, enclosing between them the fibrous or tendinous material which imparts to the valve its strength, its capacity to resist strain, and to perform the function which it is intended to fulfil.

If the inflammation does not commence in the former, it must begin in the latter; for there is no other structure to be affected. And there is every reason to believe that the primary seat of rheumatic endocarditis is the fibrous structure of the rings and valves, and not their endocardial covering.

We have seen that the rheumatic poison acts chiefly on those fibrous structures whose function it is to resist strain; and that the greater the strain the greater the liability to the action of that poison. In this we found the explanation of the tendency of that poison to affect the valves of the left, rather than those of the right, side of the heart.

The part of the valve whose function it is to resist strain, is not its external endocardial covering, but the fibrous structure which that encloses. The fibrous structure of the valve is, therefore, the part on which we should expect the rheumatic poison to act primarily and chiefly. And so, in fact, it is found to be.

The stage of rheumatic endocarditis which not only precedes the evidence of inflammation of the endocardial covering of the valves, but also precedes and gives rise to the valvular friction which induces that inflammation, is the stage of inflammatory thickening of their subjacent fibrous texture.

Rheumatic endocarditis consists primarily and essentially in inflammation of the fibrous texture of the interior of the heart.

Were the morbid change limited to this, the results, though serious enough, would be much less serious than they are. Unfortunately it is not so limited.

The inflammatory process which takes place in the valvular fibrous tissue, gives rise to multiplication of its cellular elements, and consequent thickening of the valve. Normally the valve is so perfectly adapted to the size of the orifice which it is intended to close, that, in the act of closing, its segments come into perfect and firm contact without any friction. They are firmly pressed against each other, but they do not rub.

But if the segments of the valve be thickened, it is evident that they must come in contact sooner than they ought. The size of the orifice to be closed being unchanged, and the force which closes it remaining the same, these thickened segments must come in contact before the closing force is expended. The continued operation of that force after the segments of the valve are in full contact, must lead to further movement of the segments. Normally their movement is completed at the moment of perfect and close contact; but here it is continued for an appreciable time after that event—with the necessary result of causing the valvular segments to rub against each other at the point of contact.

To put it otherwise. The swelling of the subjacent fibrous textures of the valves, necessarily elevates, and makes more prominent, the superficial covering of the swollen part. As the segments of the valve close, the unnaturally prominent endocardial covering of each comes into abnormally early contact with the opposing segment. The continuance of the act of closure, and therefore of valvular movement, after such contact is complete, necessarily causes these elevated surfaces to rub against each other. And thus is produced the friction which gives rise to inflammatory change in the external endocardial coat of the valve. The rubbing against each other of the abnormally elevated coats of the segments of a valve, produces friction and inflammatory change in the valvular endocardium, just as the rubbing of a valvular vegetation against the endocardial lining of one of the heart's cavities, produces friction and inflammatory change at the point at which it comes in contact with that membrane.

When rheumatic inflammation attacks the fibrous rings of the cardiac orifices, it produces there the same thickening as when it has its

seat in the valve; but thickening of the fibrous texture of the rings produces no such rubbing as takes place when the segments of the valves are thickened: there is not, therefore, the same evidence of inflammation of the lining membrane. The sole result is thickening of the fibrous ring, and consequent narrowing of the orifice—more or less stenosis—causing some obstruction to the onward flow of the blood.

The primary action of the rheumatic poison may be on the valves, on the fibrous rings, or on both. It is more commonly on the valves than on the rings, probably because the former are subject to greater strain than the latter. The most important fact for us to bear in mind is that *rheumatic endocarditis is primarily and essentially a disease of the fibrous structures of the heart.* It is, therefore, limited to that portion of the endocardial contents in which these structures exist. The small portion of the lining membrane of the heart which covers the fibrous valves, is very frequently inflamed: the much more extensive portion which lines the heart's cavities, suffers rarely, if ever. The sole difference between the two is, that the one is, and the other is not, in direct contact with the fibrous textures.

The lining membrane of the heart differs in structure, in nature, and in function, from that which invests it externally. Error and misconception have arisen from not recognizing this; and from regarding endocarditis as bearing to the endocardial lining membrane, the same relation that pericarditis bears to the pericardial investment.

There is little or no analogy, either physiological or pathological, between the two membranes. In acute rheumatism, extensive and general inflammation of the outer investing membrane of the heart is common: such inflammation never occurs in the lining membrane. Injury to it is secondary to change originating in the fibrous textures, and is limited to those parts of it which are in immediate contact with them.

The function of the endocardial lining is, by presenting a smooth surface to the liquid blood, to facilitate its onward flow. It has exactly the same part to perform as the lining membrane of the arteries, with which it is structurally continuous. Neither in the heart nor in the arteries does this membrane show the least tendency to take on inflammatory action: and when inflammation does occur in it, it shows no tendency to spread. The irritation produced by the rubbing of a valvular vegetation against the lining membrane of the ventricle, may be

so great as to cause ulceration at the point of contact; but the mischief is limited to this point, and shows no tendency to extend beyond it. There is no such disease as acute general inflammation of the endocardium. The membrane has no vessels, and inflammation cannot spread over its surface, as it does over that of the vascular pericardium.

In further exemplification of the view that rheumatic endocarditis is primarily a disease of the fibrous textures of the heart, it is to be noted that, in the aortic valves, early evidence of inflammatory mischief is found, not all over the seat of contact of the segments, but at one particular part of it. That part is the line of fibrous tissue on which the greatest strain falls.

A segment of the aortic valve consists of a duplicature of the endocardial lining membrane, enclosing within it the fibrous structure. At the centre of its free border is an elevated fibro-cartilaginous nodule—the *corpus Arantii*. Bands of fibrous tissue stretch across the valve to this nodule, from the border of valvular attachment to the aortic ring. Some of these run along its free surface. Others spread out over the body of the valve, and come to a point, as it were, at the corpus Arantii. Between the fibres of the free margin, and those of the body of the valve, there is, on each side of the nodule, a small space over which no fibres run. This space, called the *lunula*, consists simply of a duplicature of the endocardial lining. It is the thinnest part of the valve. In the act of closure, the three segments of the valve are thrown together into the middle of the aortic outlet, and the three corpora Arantii come into contact at its centre. The three lunulæ also come into contact; and are firmly pressed against each other by the aortic column of blood. They are all equally pressed down by this column; but the pressure thus exercised on each individual segment, is counterbalanced by the counter-pressure on its other side of the two remaining segments. Thus this thin portion of the valve is freed from strain; for the greater the pressure of the blood column, the more perfect the contact of the lunulæ, and the greater the counter-support which they give each other.

The part on which the strain falls, is the thicker fibrous portion of the valve which bounds the lunula below. The strain begins where the counter-pressure of the opposing segments ceases. "The force of the

reflux is sustained by the stouter and more tendinous part of the valve."[1]

This stouter and more tendinous part it is which suffers in acute rheumatism. The lunula is not affected. The granulations which are formed on the surface of the endocardial lining in the earlier stage of inflammation of that membrane, are limited to the convex surface of the line of fibrous tissue which passes from the attached border of the valve to the corpus Arantii, and which bounds the lunula below. (Fig. 1.) This band is at once the lowest part of the seat of valvular contact, and the highest part of the seat of valvular strain. Above it, except perhaps at the fibrous free edge of the valve, there is no strain: below it, there is no contact. It is the seat of strain; therefore its fibrous tissue is the seat of rheumatic inflammation. It is the lowest line of the seat of contact; therefore its endocardial covering is the seat of friction, when rendered unduly prominent by thickening of the subjacent fibrous tissue.

In the mitral valve there is no lunula; the whole structure is equally strained; and no one part is weaker than the rest. A weak point would be very liable to give way, for the strain on this valve is both greater, and more equally diffused over its surface, than is the strain on the aortic. In this latter valve there is only the blood pressure to be resisted: but in the case of the mitral there is both the blood pressure and the strain of the tightened chordæ tendineæ.

The whole valve and the fibrous ring may be the seat of inflammatory thickening: but here, as in the aortic valve, the evidence of inflammatory change in the endocardial lining membrane is limited in its early stage to the auricular surface, and to the line of contact of the valvular segments. (Fig. 2.) In other words, in the mitral as in the aortic valve, the granulations which are formed in the earlier stage of inflammation of the valvular endocardium, are formed at that line which is at once the seat of strain and the point of contact. It is the seat of strain; therefore its fibrous tissue is the seat of rheumatic inflammation. It is the point of contact; therefore its endocardial covering is the seat of friction, when rendered unduly prominent by inflammatory thickening of the subjacent fibrous tissue.

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[1] Quain, op. cit.

Microscopic examination of the affected portion of valve, confirms this view of the nature and seat of the morbid change. On making a section of one of these granular nodules, and submitting it to such examination, it is found that the seat of swelling is the deep layer of fibrous tissue, and that the superficial lining of the valve is merely raised up by the multiplication of the cellular elements of the subjacent fibrous texture. "If a valve with these nodules be cut for the microscope across the plain of its curtain, so as to show a section down through one of the small nodules, this will be found to be composed of a simple cloudy swelling of the tissue of the valve through a multiplication of the cellular elements in its fibrous structure, which here and there by its excess raises the surface into a little hillock. If the hillock takes the form of a distinct projecting grain, you will always find on the top of it a cap of fibrine separated from its substance by a line which the microscope defines very clearly. This cap of fibrine differs in composition from the hillock itself, though the difference is more easily seen than described, for the organization in both is very low; but the fibrine is almost structureless, while the hillock of swollen valve substance shows the regularly placed nuclei of fibrous tissue." [1] (Fig. 3.)

Fig. 3.—Acute Endocarditis.—A granulation from the mitral valve, showing a fibrinous coagulum upon the surface of the granulation. × 10. (Rindfleisch).

The cap of fibrine here described, is fibrine which is deposited directly from the blood on the roughened surface of the endocardium, just as it would be deposited around any foreign body. The true seat of the inflammation, is the deeper fibrous tissue of the valve.

The symptoms and signs of rheumatic endocarditis vary with the seat of the disease, and the severity of the attack. Occurring, as it does, in the course of acute rheumatism, any febrile disturbance to which it may give rise is apt to be lost in that attributable to the joint inflammation. That endocarditis slightly raises the temperature, there

[1] Wilks and Moxon, op. cit.

can be no doubt; but the invasion of fresh joints has a more marked effect in that way; and as the cardiac complication generally occurs at a stage of the illness when fresh joints are apt to suffer, it is seldom possible to say how much of the abnormal rise is due to the heart affection. Inflammation of the endocardium may cause less general disturbance than inflammation of a joint; while its local effects may be so slight as to be imperceptible to the patient.

The symptoms special to it are subjective and objective. The subjective are not commensurate with the serious nature of the ailment. They vary with the severity of the attack. Frequently they are altogether absent. In very acute cases there may be pain in the cardiac region; the heart's action may be disturbed and rapid; the breathing accelerated, oppressed, or even labored; and the patient very anxious. If both aortic and mitral orifices and valves are acutely inflamed, such are apt to be the symptoms. But in such acute cases the muscular substance of the heart is generally more or less involved in the inflammatory mischief, and it is probable that some of the symptoms are due to this, as much as to the endocardial inflammation. Moreover, the pericardium is also liable to be inflamed in such severe cases.

When the inflammation is less severe and extensive, and limited to the endocardium, there may be no more than a sense of uneasiness in the region of the heart, with little or no disturbance of the breathing, or of the cardiac action. In many cases, indeed in the majority, subjective symptoms are entirely absent; and the sole indication of the existence of the endocarditis, is the altered character of the heart's sounds—the alteration generally consisting in the development of one or more murmurs.

The absence of subjective symptoms makes it necessary that the heart should be frequently examined. At every visit this should be done. If in a case of acute rheumatism, in which we are sure that no endocardial murmur existed at our last visit, we find one developed at our next, we may be certain that it is due to a recent endocarditis.

It has been said that such murmurs may be of anæmic origin. I do not think that nowadays they ever are so. They may sometimes have been so in the old days of free bleeding; but in the absence of such treatment, it is impossible for an anæmic murmur to be developed in the short time that suffices for the production of those which we are

now considering. In acute rheumatism an anæmic murmur could scarcely be developed till late in the case; those now under consideration generally appear in the early stage of the disease. Moreover, anæmic murmurs are basic; those due to rheumatic change in the endocardium are more often mitral; and when basic, are all but invariably limited to the aorta.

The physical signs are the only certain diagnostic indications of the existence of endocarditis.

In the aortic valve we have seen that the morbid change consists in thickening of its segments, and in roughening of their convex surfaces. (Fig. 1.) During the systole of the heart these segments are thrown against the walls of the aortic outlet. Thickening of their fibrous texture must, therefore, cause a diminution of the calibre of this outlet—a diminution which is directly as the extent of the morbid change; while the deposition of fibrine on the surface of the valve, not only further diminishes the aortic outlet, but, by presenting to the blood a roughened surface, interferes with the naturally smooth and easy passage of that fluid from the heart into the great vessels. The result, and the physical evidence, of this state of matters, is the development of a systolic murmur, loudest at the base, and transmitted into the aorta.

If one or more of these segments should be so altered as to render due closure of the valve impossible, some of the blood regurgitates back into the ventricle from the aorta, and there is developed a diastolic basic murmur, transmitted downwards into the heart, and most distinct at mid-sternal region. But such change, when it occurs, is usually one of the later after effects of the valvular lesion.

In the mitral valve the morbid change consists in thickening of its structure, and in roughening of its auricular surface at the line of contact of its segments. (Fig. 2.) But these changes in the mitral valve do not produce on the cardiac circulation the same effect as similar changes in the aortic. In the latter the thickened valve is thrown against the wall of the ventricular outlet, so as to form part of its circumference; and its roughened surface is thus presented to the direct current of the blood as it passes through that outlet. In the former the valve is suspended, as it were, in the ventricular cavity, away from the

auricular outlet while the blood is flowing through it. It may have its fibrous textures thickened, and its endocardial covering roughened, without causing any change in the condition of the orifice which it is intended to close, and without producing any obstacle to the onward flow of blood, such as results from inflammatory thickening and roughening of the aortic valve.

But such morbid change in the mitral valve produces more serious disturbance of the valvular function than does a corresponding change in the aortic. For in the latter the thickening is partial; the lunulæ are not affected; and so long as they come well into contact the valve continues to perform its function.

But in the mitral valve there is no lunula; the whole segment is thickened. Here thickening means loss of mobility, loss of pliability, and consequent loss of adaptability—a condition which is exaggerated by the roughening of the surface of the valvular segments at their line of contact. The result is, that the two segments of the valve either do not act with sufficient rapidity, or do not come into close and perfect contact; a certain quantity of blood regurgitates back into the auricle; and there is developed a mitral systolic murmur.

Though the most common, this is not the only murmur which may be developed at the mitral orifice during a rheumatic attack. A præsystolic murmur, the evidence of narrowing of the mitral orifice, may also be noted with, or without, a coexistent systolic one. The narrowing of the auricular outlet which gives rise to this murmur, results from inflammatory thickening of the fibrous textures around that outlet. This thickening is produced by rheumatic inflammation of the fibrous texture of the auriculo-ventricular ring, just as thickening of the valve is produced by similar inflammation of *its* fibrous elements. Inflammation of both the fibrous rings and valves, indicates a more decided action of the rheumatic poison on the endocardium, and a more severe attack of endocarditis, than inflammation of only one of them. Cases in which there is this general affection of the fibrous textures of the endocardium, are more apt to be accompanied by disturbed and irregular action of the heart, and by increased frequency of respiration, than are those in which the valves alone suffer. But this general affection of the fibrous textures of the endocardium may exist, and all these objective indications of its existence may present themselves, without any

pain or uneasiness about the heart, or any subjective symptom directly referable to that organ.

This absence of pain in rheumatic inflammation of the fibrous textures of the heart, is one of the chief points of distinction between it and similar inflammation of the fibrous textures of the joints.

Another distinction, and one of much more serious import, is that the results of rheumatic inflammation of the fibrous textures of a joint, are generally transient, and perfectly recovered from; while those of like inflammation in the fibrous textures of the heart, are apt to be permanent, and never recovered from. Why is this? The poison which produces the inflammation is the same in both. The tissue on which it acts has in each the same structure, and a similar function. Why, then, should the results be so different?

The temporary character of the injury to the loco-motor fibrous textures, has been ascribed to the absorbent effects of the pressure exercised on the effused products by the surrounding solid structures. The permanence of the damage to the vasculo-motor fibrous textures has been ascribed to the absence of such pressure. "The permanence of the injury in the case of endocarditis is simply due to the want of counter-pressure. In the joints the swollen membranes are pressed against the other solid structures as soon as the liquid effusion is removed. This pressure causes absorption of all the new products, whereas in the heart there is no direct pressure of solids against the inflamed valves, which stand freely in fluid blood, so that the new products persist."[1]

It seems to me that a more probable and adequate explanation of this unfortunate difference, is to be found in the fact that when the fibrous textures of a joint are inflamed, they get perfect rest, and are thus placed in circumstances favorable to complete recovery: while the fibrous textures of the heart not only get no rest, but, from the greater frequency of the heart's action, are called upon to do an increased amount of work. They are thus placed in circumstances which make complete recovery all but impossible.

Acute cases of rheumatism, in which the fibrous textures of the joints are smartly inflamed; in which there is a considerable amount of

[1] Wilks and Moxon, op. cit.

thickening and effusion; and in which complete rest is given to the inflamed textures, are also those in which these textures are most fully and speedily restored to their natural state.

In chronic cases in which the inflammation is slight, in which the patient continues to go about, and in which, therefore, the inflamed ligaments and tendons do not get rest, these textures are more apt to be permanently thickened.

If pressure were the agency which removed the effusion, it ought to disappear more speedily in these chronic cases than in the acute; for the act of locomotion supplies this factor, and would lead to speedy absorption of the effused products, and early restoration of the fibrous textures to their normal state.

The long duration of the thickening and stiffness of the joints in such cases, is to be explained in the same way as the persistent nature of the cardiac damage. Absence of rest leads to imperfect recovery and permanent injury.

It is extremely doubtful if a heart whose fibrous textures have once been thickened by inflammation, and whose endocardial lining has once been roughened, ever recovers its normal condition. For the fibrous textures continue to be strained, and the roughened surfaces of the segments go on rubbing. Irritation is thus kept up after the primary inflammation has disappeared; the thickening of the fibrous textures becomes chronic and permanent; and fresh rheumatic attacks add to the mischief.

With the advance of time the morbid change becomes more marked: the valvular segments become contracted and misshapen; the cardiac circulation is more disturbed; the muscular walls of the heart hypertrophy; its cavities dilate; and the sufferer enters on a prolonged course of misery, whose only termination is death.

CHAPTER XIII.

PERICARDITIS.

Between the pericardium of the anatomist, and that of the pathologist, there is no difference. Rheumatic pericarditis consists in rheumatic inflammation of the investing membrane of the heart. As already explained, such inflammation is most common in acute cases, and in young subjects.

Of all the serous membranes of the body, the pericardium is the only one which invests an organ having free and active movements. So far as functional activity is concerned, the pericardium is as much above other serous membranes, as the valves of the left side of the heart are above those of the right, and the fibrous tissues and serous linings of the large joints above those of the small. In its liability to rheumatic inflammation the pericardium is in the same position as the serous lining of a large joint.

Pericarditis occurs in different degrees of severity. The whole membrane may be the seat of acute inflammation: or only a small part of it may be affected. According to its extent and severity are the symptoms to which it gives rise. As a rule, subjective symptoms are more marked than in endocarditis.

In acute and severe cases, pain in the region of the heart is generally present at the outset, and is often the first thing complained of. Usually it is increased by pressure over the heart, or in the epigastrium. The patient is restless and distressed; his countenance has an anxious expression; the breathing is quickened; there is generally a short frequent cough; the heart's action is vigorous and rapid—maybe tumultuous, violent, and irregular. On auscultation there is heard the friction sound produced by the rubbing against each other of the roughened pericardial surfaces.

But the heart symptoms are not always so distinct in these acute cases. Occasionally their place is taken by nervous symptoms so marked that the case is apt to be mistaken for one of cerebral rheuma-

tism. The onset of the pericardial inflammation may be ushered in by delirium; and delirium, stupor, and coma, may be its characteristic symptoms throughout. From beginning to end there may not be a single subjective symptom of cardiac disturbance—nothing, in short, but the evidence of cerebral disturbance. The occurrence of head symptoms in acute rheumatism is always a reason for suspecting and carefully examining the heart.

The following case, recorded by Andral,[1] is a good illustration of the manner in which acute pericarditis may simulate inflammatory mischief in the nervous centres:—

"Symptoms of Meningitis. Acute inflammation of the pericardium."

Case I.—"A woman, aged 26, the mother of two children, and who had recently had a miscarriage, was admitted into la Charité early in the year 1820, in such a state of delirium that no information could be got regarding her antecedents. The delirium was remarkable for the obstinate taciturnity by which it was accompanied. When asked a question, the patient looked fixedly at one without answering; the face was pale; the lips, separated from each other, and agitated from time to time as by a convulsive trembling, allowed the tongue to be seen, moist and white. The pulse was frequent and small, but regular; the skin rather cold. During the next two days there was frequent bending backwards of the head, sudden raising of the trunk at intervals, and *subsultus tendinum*. The patient spoke, and appeared to understand what was said to her, but was quite incoherent in what she said. The face was very pale; the pulse very frequent, and intermittent. On the fourth day after admission the delirium ceased; the patient complained only of great weakness; the muscles of the face were agitated by almost continual convulsive movements; and the upper extremities were affected from time to time with an almost tetanic rigidity. On the fifth day the delirium returned, the features were distorted: during the course of the day the patient became comatose, and died in the evening."

On *post-mortem* examination it was found that "there was no appreciable change in the color or consistence of the brain, spinal cord, or their membranes. The digestive canal, opened throughout its whole

[1] Andral, Clinique Médicale, Tome I., p. 34.

extent, presented only a slight injection here and there. The other abdominal viscera were free from lesion. The lungs were slightly congested posteriorly. The substance of the heart presented no trace of morbid change: the vessels entering and issuing from it, were also healthy. But the pericardium was covered with a lymphy deposit (par des concrétions albumineuses), which stretched at many points like a soft bridle from the visceral to the parietal surface. Effused into its cavity, too, were several ounces of a greenish and floeculent serum."

In subacute pericarditis the subjective symptoms are less marked. There may be no more than a sense of uneasiness about the heart, with some increased rapidity of its action. It is on the auscultatory signs that we depend for a diagnosis.

In some mild cases there are no subjective symptoms whatever—nothing but the objective pericardial rub to point out the existence of the disease.

Some cases of pericarditis there are, too, in which the inflammation is limited to that portion of the membrane which surrounds the great vessels at the base of the heart; and in which there is during life no evidence, either subjective or objective, of its existence. In the *post-mortem* room it is that the occurrence of this very limited form of the malady is occasionally demonstrated in the persons of those who have died of some other complication.

The earliest stage of inflammation of the pericardium consists in hyperæmia of the membrane. It cannot be said that this stage has any specially characteristic symptoms or physical signs. But in acute cases it is accompanied by increased vigor and energy of the heart's action. Without producing any *bruit*, this increased vigor imparts to the first sound of the heart an exaggerated ring or tone, which may be sufficiently marked to enable us to suspect, if not actually diagnose, commencing inflammation of the pericardium. This "tension sound," as it has been called, may be regarded as the earliest objective evidence of the onset of pericarditis. It is only in acute cases that it is observed; and in them the first stage of the disease, during which alone it is heard, lasts for so short a time that this sign may readily escape detection. Even when observed, it is soon thrown into the background by the more striking and important indications of the following stage.

The second stage comes in quick succession to the first. It is characterized by the effusion of lymph, and the formation of a fibrinous layer of new material, on the surface of the inflamed membrane. It is at this period that the signs and symptoms of the disease come to the front, and that its existence is generally diagnosed. The new material which is formed on the surface of the pericardium produces a marked alteration there. Instead of a smooth, glistening surface, allowing the visceral to glide gently and easily over the parietal portion of the membrane, there is a coating of lymph which is so soft that its surface gets roughened by the friction to which it is subjected, and becomes ragged and shaggy in appearance. The rubbing against each other of the thus roughened surfaces of the pericardium produces the "to and fro" friction sound characteristic of the disease. This sound is generally double, but may be single, and then is usually short and with difficulty distinguished from an endocardial murmur. It is generally heard first near the base of the heart; but it may be distinct over the whole organ. It is superficial in character, like a pleuritic rub; but easily distinguished from that by its situation, and by its being independent of the respiratory movements. There is no increase of cardiac dulness. This is the stage at which any subjective symptoms which may exist are usually felt.

The morbid process may go no further than this. The inflammation may decline; the lymph may be reabsorbed; and the pericardium be restored to its natural state. Or the two roughened surfaces may adhere together to a greater or less extent.

In acute cases there is generally a third stage, characterized by the effusion of serum into the sac of the pericardium.

A certain amount of fluid is thrown out during the second stage, at the same time as the lymph. The quantity may be so small that it gives no physical evidence of its existence, and is quickly absorbed when the inflammation subsides.

The presence of a larger quantity gives very decided evidence of its existence. It separates the visceral from the parietal layer of the pericardium. Rubbing of these surfaces against each other thus becomes impossible; friction ceases to be heard; and any pain which there may have been, disappears. The area of cardiac dulness is increased. If the sac of the pericardium be quite full, the region of dulness has the triangular shape of that sac—with the apex above and the base below.

The dulness extends to the left of, and beyond, the apex point. The heart's impulse is not felt as in hypertrophy of the organ. The sounds are distant and indistinct. The pulse is quick and feeble—maybe irregular. There is increased frequency of respiration; and the patient may be in considerable distress.

Under proper treatment, and in the absence of other complications, the fluid is generally absorbed. As it diminishes in quantity, the region of cardiac dulness also decreases. The two layers of the still roughened pericardium once more come into contact; and friction is again heard for a day or two. Here, as in the case in which recovery takes place at the end of the second stage, the friction gradually disappears, and ultimately everything seems to return to its natural state—recovery being apparently perfect. It is doubtful, however, if the pericardium ever quite regains its natural condition. It may possibly do so in some cases; but in most instances more or less extensive adhesions are formed between its two layers. Where the inflammation has been severe, such adhesions are formed over the whole surface of the heart, and the sac of the pericardium is obliterated.

Such obliteration has been regarded by some as a source of much embarrassment to the heart's action, and a cause of hypertrophy and dilatation of that organ. By others it has been said to produce some degree of atrophy of the heart. While a third set of observers maintain that an adherent pericardium gives rise to no symptoms during life, and to no morbid change in the muscular substance of the heart.

It is probable that the age and mode of life of the patient have much to do with the variety of the results noted by different observers; for if the function of the pericardium be to facilitate free movement of the heart, obliteration of its sac will cause most disturbance in those in whom the movements of that organ are most free and active—in young and excitable persons, and in those whose habits or tastes lead them to take much exercise, and so increase the vigor and frequency of the heart's action.

The function of the pericardium is to provide for the free and active movements of special occasions, and unusual efforts. If such occasions do not arise, and such efforts are not made, the obliteration of its sac causes no embarrassment, and no change in the heart. The ordinary work of that organ can be quite well done without the pericardium;

and so long as this work is not unduly increased, and extraordinary efforts are not required, no harm results from the obliteration of its sac. It is for the free movements of special occasions that it is required. "The free motion of the heart within the pericardium is required in health, not so much to meet the necessities of the circulation in its tranquil and ordinary condition, as to provide for the contingency of excited action, and to give abundant scope for the smooth and painless motion of the heart under those circumstances in which the habitual equilibrium of the circulation is disturbed."[1]

It is doubtful if a severe attack of pericarditis, resulting in obliteration of the sac of the pericardium, ever occurs without the muscular structure of the heart participating more or less in the morbid process. The evidence of its being affected would be lost in the more prominent signs of the pericarditis. Such myocarditis might lead to subsequent change in the heart—a change which would not unnaturally be attributed in the *post-mortem* room to the obliteration of the pericardium.

Occasionally the fluid effused into the pericardial sac becomes purulent; but such an occurrence is much more rare than in inflammation of the pleura.

There is one fact in the history of rheumatic pericarditis which has a more important bearing on the pathology of the disease than any other circumstance noted during its course. This fact is that *the disease almost always commences in the visceral layer of the pericardium, and at the base of the heart.*

The evidence of this is as follows:—

1. In slight and circumscribed attacks, the inflammatory change is, as a rule, confined to this portion. Affecting only the visceral layer, and only a small part of it, there may be no physical signs or symptoms by which its existence may be diagnosed. But we know that such slight attacks do occur; for in the *post-mortem* room it is not uncommon to find some thickening and opacity, the result of inflammation of this part of the pericardium, without any evidence of the disease having existed elsewhere.

2. In cases in which the disease spreads over the body of the heart,

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[1] On the Favorable Terminations of Pericarditis, by W. T. Gairluer, M.D., Edinburgh Monthly Journal of Medical Science, 1851.

and affects both layers of the pericardium, the friction sound is generally heard first near the base.

3. In cases in which death takes place in the early stage of the disease, it is found that while that part of the membrane which is situate over the body and apex of the heart is merely hyperæmic—is still in the first stage of inflammation,—that which surrounds the origin of the great vessels at the base has reached the second stage, and is covered with shreds of lymph. "In ordinary acute pericarditis the earliest stage is seen as a minute injection of its vessels, causing a blush of redness, which close observation resolves into a beautiful red network. This injection is almost a certain proof of pericarditis, but when you see it you should look at the base of the heart, about the great vessels, where you will always find some shreds of inflammatory lymph."[1]

Is there any possible explanation of these facts—any reason why the rheumatic poison should act primarily and chiefly on this part of the pericardium? There is no structural peculiarity to account for it. It cannot be due to greater functional activity; for movement is freer at the apex than at the base. *The only peculiarity of that portion of the pericardium which seems specially liable to rheumatic inflammation, is that it is situate over, and in near contact with, the fibrous textures of the heart*—in near contact, that is, with that particular portion of the cardiac structures, which is specially liable to suffer from the action of the rheumatic poison. The inference is inevitable, that inflammation of the pericardium may be due, not to the direct action of the rheumatic poison on that membrane, but to the extension to it of an inflammatory process originating in the subjacent fibrous textures.

We have already seen that inflammation of the inner lining membrane of the heart is limited to that part of it which is in direct relation with the fibrous rings and valves, and is secondary to inflammatory change in these structures.

There is not a little evidence to show that in many cases, if not in all, inflammation of its outer investing membrane, has primarily a like limitation and a similar pathology.

The fact cannot be too strongly insisted on, that the membranes which line the interior and exterior of the heart, are essentially different

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[1] Wilks and Moxon, op. cit., p. 98.

both in structure and function: they have indeed nothing in common but their membranous nature and cardiac situation. The endocardium has no vessels, and is therefore not liable to inflame. The pericardium is very vascular. It is the analogue in the heart of the lining membrane of the joints. Its function is to facilitate the free and active movements of a solid structure. Like the lining membrane of the joints, it is very susceptible to inflammation, and the process is liable to spread from one point over the whole surface.

We have already seen reason to believe that inflammation may extend from the fibrous ligaments to the synovial membrane of a joint. There is also reason to believe that it may extend to the pericardium from the fibrous textures of the heart. Indeed, what was said regarding the extension of the inflammatory process to the synovial membrane from the fibrous structures of the joint, is equally applicable to the case of the pericardium. It is in more or less acute cases that inflammation of the synovial membrane, and effusion into the joint, take place: it is in such cases also that inflammation of, and effusion into, the pericardial sac, occur. The more acute the case the more marked the synovitis and joint swelling. The more acute the case the more likely is there to be inflammation of, and effusion into, the sac of the pericardium.

In chronic and in mild subacute cases the fibrous structures of the joints are inflamed, and there may be some thickening of their texture; but, as a rule, there is no inflammation of the synovial membrane, and no effusion into the joint. In similar cases there may be some inflammation of the fibrous structures of the heart; but, as a rule, there is no extension of the inflammation to the pericardium, or effusion into its sac.

CHAPTER XIV.

MYOCARDITIS.

INFLAMMATION of the muscular walls of the heart, is an ailment which owes its recognition to *post-mortem* observation.

Numerous cases have been recorded in which these walls have been found, after death, to be the seat of inflammatory softening, induration, or even suppuration. With this evidence of myocarditis there has usually been associated the usual *post-mortem* signs of endocarditis, of pericarditis, or of both. The existence of this association, and the rarity of *post-mortem* evidence of myocarditis except in combination with inflammation of the membranes, has led to the not unnatural belief that inflammation of the muscular substance is secondary to that of the membranes, and results from the direct extension to it of an already existing inflammation of one or both of these.

Myocarditis occurring independently of endo-pericarditis is described by Walshe [1] as "an affection, to say the least, of extreme rarity."

Peacock [2] says that myocarditis "is rather interesting in a pathological point of view than practically important. It probably always occurs in connection with one or both the other forms of disease," *i.e.*, endocarditis or pericarditis.

"Inflammation of the heart substance is frequently set up in the layers contiguous to an inflamed endocardium or pericardium." [3]

"Inflammation of the muscular substance of the heart rarely occurs except in connection with peri- or endo-carditis. In pericarditis a greater or less thickness of the muscular walls in contact with the inflamed serous membrane is often distinctly implicated; and there is no doubt that their inner aspect may be similarly involved during the course of an attack of endocarditis." [4]

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[1] Diseases of the Heart, 4th ed., p. 263. 1873.

[2] St. Thomas's Hospital Reports, 1875, p. 12.

[3] The Theory and Practice of Medicine, p. 39, by F. F. Roberts, M. D., F.R.C.P., 3rd ed. 1877.

[4] The Theory and Practice of Medicine, p. 516, by J. S. Bristowe, M.D., F.R.C.P. 1876.

Such are some of the most recently expressed opinions. They accurately represent the view generally entertained by pathologists.

But when we come to examine the grounds on which this opinion is based, we find that they are scarcely adequate to its support, and that the view that myocarditis is secondary to, and dependent on, prior inflammation of the endocardium is one which cannot be maintained.

When considering the subject of endocarditis, we saw that the lining membrane of the heart is a non-vascular structure, in which inflammation cannot, and, as a matter of fact, does not, spread. If the endocardium cannot itself be the seat of inflammation, it is impossible for that process to extend from it to other structures.

The morbid change which takes place in it during the course of acute rheumatism, is secondary to change in the subjacent fibrous tissue, and is limited entirely to that part of the membrane which is reflected over the fibrous valves and rings. It never extends to the part which lines, and is in contact with, the muscular substance, and from which alone it could extend to that substance.

Limited as the morbid process thus is, and showing no tendency to spread, it is in the highest degree improbable, if not actually impossible, that inflammation should ever extend from the endocardium to the muscular substance of the heart.

In cases in which myocarditis coexists with inflammatory or ulcerative change in the muscular portion of the endocardium, the course of events is the reverse of what is usually supposed—the myocarditis is primary, the endocardial mischief secondary.

The only part of the endocardium which suffers in the course of acute rheumatism, is that which is reflected over the valves and rings; and even here, mechanical friction of the segments, consequent on inflammatory thickening of the subjacent fibrous textures, seems necessary to the production of the change. What is chiefly to be noted is that the change in the endocardium is consequent on a prior change in the fibrous tissues. The inflammatory process spreads from fibrous tissue to membrane, and not from membrane to fibrous tissue.

When the endocardium and the muscular substance are involved, we have to deal with a similar course of events: the extension is from muscle to membrane, and not from membrane to muscle.

A consideration of the pathology and mode of production of rheu-

matic endocarditis, lends no support to the view that inflammation ever extends to the muscular substance of the heart from its lining membrane.

It is different with the pericardium. Here we have to deal with a membrane which is richly supplied with blood-vessels, which readily takes on the inflammatory process, and in which that process very readily spreads. That inflammation may, and sometimes does, extend to the pericardium from the muscular substance, there can be no doubt (it was so, for instance, in Mr. Stanley's case, to be presently related). But there is also good reason for the belief that the morbid change sometimes takes the reverse course, and extends from the pericardium to the heart; for in fatal cases of pericarditis, it is sometimes noted that the layer of muscular tissue in immediate contact with the inflamed membrane, is the seat of more decided inflammatory softening than that which lies nearer the endocardium. Sometimes it is the only part which is distinctly softened.

But myocarditis occurs independently of pericarditis; and may involve the whole thickness of the cardiac walls. It is then situated chiefly at the base of the heart, and is usually regarded as due to extension of inflammation from the endocardial lining. But that we have seen to be not only inconsistent with the facts of the case, but to be all but practically impossible. How, then, is it produced? There are two possible explanations. One is to regard it, as we regard all cases of inflammation of the endocardium, and many cases of inflammation of the pericardium, as an extension of the inflammatory process from the fibrous textures. The other is to regard it as primary, as due to the direct action of the rheumatic poison on the muscular substance.

1. The muscular fibres of both auricle and ventricle are attached to the fibrous ring which surrounds, and forms, the auriculo-ventricular opening. This ring is also the tendinous attachment of the cardiac muscles. If inflammation spread to these muscles from any structure, it is most likely to be from that with which they are most intimately connected, provided only that it is the seat of inflammation. The muscular fibres of the heart are most intimately connected with the fibrous rings—so intimately, indeed, that it is difficult to draw a pathological line between them. These rings are a common seat of rheu-

matic inflammation. It is, therefore, in the highest degree probable that, if inflammation spreads from them at all, it will be to the muscular substance. Inflammation may extend even more readily from the fibrous structure of the rings to the very vascular muscular walls, than from the fibrous structure of the valves to their non-vascular endocardial covering. In connection with this point it is to be noted, that localized myocarditis is most common in the neighborhood of the fibrous rings.

But myocarditis is not always so localized; and the question arises whether the disease may not sometimes be primary—due to the direct action of the rheumatic poison on the cardiac muscles.

2. That muscular tissue is sometimes the seat of rheumatism is generally admitted. Most authors describe a form of the disease which, from its situation, is called "muscular rheumatism." Such rheumatism may coexist with the more regular and distinctive arthritic form of the malady.

When considering the action of the rheumatic poison, we saw that the structures specially liable to be affected by it are those which are habitually subject to stretching and strain. There are not very many muscles of which it can be said that they are habitually liable to be stretched. But there are some. The chief of these are the posterior muscles of the spine—those situate between the occiput and the pelvis. These muscles are more or less stretched every time that we stoop or bend. The points at which the stretching is greatest are those at which the spine moves most freely—the neck, and the lumbar region. These are the very points at which rheumatism of the muscles is most apt to be developed. The muscles of the neck and of the loins are at once more liable to be strained, and more subject to rheumatism, than any other voluntary muscles.

But of all the muscles of the body, those which are most subject to strain are the muscles of the heart. If we recognize the existence of a rheumatic affection of voluntary muscle, and of a connection between liability to strain and the tendency to rheumatism, we must also regard rheumatism of the cardiac muscles as a likely occurrence. For much more than voluntary muscles are they apt to be strained; and much more necessary is it that they, like the fibrous textures of the

joints, should be prepared to resist strain. Undue stretching of a voluntary muscle may cause pain, but does no material damage. Undue stretching of the walls of the heart may lead to most serious consequences.

Here, again, we see the difficulty of drawing a pathological line between the fibrous and muscular structures of the heart; for a force which strains and stretches the muscular walls, must also strain the fibrous rings.

There is no *a priori* reason why the rheumatic poison may not act directly on the cardiac muscles, and it is probable that it not unfrequently does so. It is equally probable that inflammation may extend to these muscles from the fibrous textures. In the former case, the inflammation is more likely to be general and involve the whole ventricle. In the latter, it is likely to be local and limited to the neighborhood of the fibrous rings.

Though a point of some pathological interest, it is fortunately a matter of no practical importance which view we take. The important point is that we should recognize the occurrence of myocarditis *independently of inflammation of the membranes;* and should look upon it, as we look upon endocarditis and pericarditis, as a not uncommon complication of acute rheumatism, and as one which may exist, either alone or in combination with inflammation of the other textures of the heart.

It would be at once more accurate for pathological, and more satisfactory for clinical, purposes, if the cardiac lesions of acute rheumatism, instead of being described under the heads of pericarditis, myocarditis, and endocarditis, were classified as pericarditis, myocarditis, and valvulitis,—by pericarditis being meant inflammation of the pericardium; by myocarditis, inflammation of the muscles and fibrous rings of the heart; and by valvulitis, what is usually described as endocarditis—inflammation of the textures of the valves.

But whatever classification we adopt, and whatever names we use, the important points for us to bear in mind are: (1) that the fibrous structures of the heart are the chief seat of the action of the rheumatic poison; and (2) that the muscular substance is frequently involved in the morbid process.

The symptoms of myocarditis are very obscure—so obscure that the

diagnosis of the disease during life is generally regarded as, at the best, a matter of inference rather than of certainty.

"I am not aware that the existence of carditis has ever been diagnosed."[1]

"There are no means by which inflammation of the muscular structure of the heart could be diagnosed during life."[2]

"It is not to be diagnosed during life except as a matter of probability."[3]

"It will be almost impossible to make a diagnosis."[4]

"Myocarditis is but seldom diagnosed during life."[5]

Such is the general opinion. I believe it to be an exaggerated expression of the difficulties of the case. That the diagnosis of myocarditis is always difficult, and sometimes impossible, there can be doubt. But it is equally certain that there are cases in which its existence can be determined with tolerable certainty.

The difficulties are great in consequence of the absence of such distinctive physical signs as are noted in inflammation of the membranes; but they are not insurmountable. They have been much increased by faulty pathological views regarding the causation of the disease. The existence of inflammation of the muscles of the heart, independently of inflammation of the membranes, has not been recognized. It, therefore, has not been looked for; and the indications of its existence are not sufficiently marked to force themselves on our notice.

We are so accustomed to trust to a physical examination of the heart for the diagnosis of morbid change in that organ, that a cardiac malady which cannot thus be readily diagnosed, is likely to escape detection. It has been so with myocarditis. The difficulty has been still further increased by the fact that in many cases subjective symptoms either do not exist, or are not such as are calculated to direct attention to the heart.

Rheumatic myocarditis, like rheumatic endocarditis, is almost en-

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[1] Walshe, op. cit., p. 264.
[2] Peacock, St. Thomas's Hospital Reports, 1875.
[3] Aitken, Science and Practice of Medicine.
[4] Schroetter: Ziemssen's Cyclopædia of Medicine.
[5] Niemeyer, Text-book of Practical Medicine.

tirely confined to the left ventricle. It may be partial, or general—involving a part, or implicating the whole thickness and extent of the ventricular walls.

1. The former is the more common. Its usual situation is at the base of the ventricle. It probably results in most cases from an extension of the inflammatory process from the fibrous structures. As there is usually a similar extension of that process to the endocardial lining, any symptoms to which the myocarditis may give rise, are lost in the more obvious indications of the valvulitis. It cannot in such a case be diagnosed during life. This is not a matter of much importance; for such limited myocarditis is not a source of danger, and the treatment applicable to the accompanying valvulitis, is equally applicable to it. The evidence of its occurrence is found in the *post-mortem* room, in the form of circumscribed patches of induration of the muscular wall of the ventricle, chiefly at the base, and generally in company with thickening and induration of the fibrous rings and valves.

2. General rheumatic inflammation of the walls of the left ventricle, like other local inflammations, occurs in varying degrees of severity. When very acute, it may give rise to such destructive change in the ventricular walls that recovery is impossible. In a mild and subacute form, it causes simply softening of the ventricular walls—a condition which may be perfectly recovered from, or may result in more or less induration of the muscular substance.

The symptoms and results of these two forms of myocarditis are so different that it will be well to consider them separately. But, though for clinical convenience considered separately, they are merely varieties of the same disease.

Acute myocarditis is a formidable disease, apt to be fatal, and apt to be overlooked. It is apt to be fatal, because of the importance of the tissue inflamed; it is apt to be overlooked, because of the obscure and even misleading character of some of its most common and prominent symptoms.

Corvisart[1] divided cases of myocarditis into two classes, the *distinct* and the *latent*,—those in which the symptoms clearly indicate the

[1] Essai sur les Maladies et les Lesions Organiques du Cœur et des Gros Vaisseaux. Paris, 1818. 3me ed.

nature of the disease, and those in which symptoms directly referable to the heart scarcely exist.

Acute pain in the epigastrium, or præcordial anguish, a sense of oppression and anxiety, embarrassed respiration, the evidence of defective aeration of the blood, without any pulmonary lesion to account for it,—such are the symptoms which may present themselves in distinct cases of acute myocarditis. Seldom, if ever, do they all exist at the same time. Now one, now another predominates. The most common are præcordial uneasiness, and evidence of defective aeration of the blood. With these there are often associated symptoms of disturbance of the sensorium.

Acute myocarditis is generally accompanied by inflammation of the endocardium or pericardium, or both. It is then part of a general carditis. The physical signs of the membranous inflammation are so obvious, that all the symptoms are apt to be ascribed to it. It is probable that the less obvious myocarditis plays a not unimportant part in the production of many of them; but how much of the patient's disturbance is due to the membranous, and how much to the muscular, inflammation, it is impossible to say.

It is a matter of course that when both the walls of the ventricle, and the membranes are inflamed, there is likely to be greater disturbance and irregularity of the heart's action, and a greater tendency to death, than when the membranes only are involved. But it is impossible to diagnose the extent of the myocarditis as we do that of the endopericarditis. All that we can say is that if, in the course of a case of rheumatic inflammation of the membranes, we find either a marked degree of cerebral disturbance, without high temperature; or evidence of defective blood purification, without any pulmonary lesion, or any serious amount of pericardial effusion, we may feel sure that the muscular substance of the heart is seriously involved in the mischief, and that death is threatened by asthenia.

The physical signs of the membranous inflammation, so predominate over any change in the cardiac sounds to which the myocarditis might give rise, that we can better diagnose the existence, and gauge the extent of this latter, by careful observation of the general symptoms, than by a physical examination of the heart.

There are cases of acute myocarditis, as of acute pericarditis, which

run their whole course to a fatal termination without any symptom directly referable to the heart; the only symptoms being those of cerebral disturbance. An admirable illustration of this is found in a case recorded by Mr. Stanley in the seventh volume of the "Medico-Chirurgical Transactions," 1816. So far as I know, it is the earliest recorded case of the kind.

Case II.—"A boy, aged twelve years, although of a delicate frame, had enjoyed generally a good state of health. On Saturday the 20th of April he was apparently quite well, having been on that day on a visit to one of his relations by whom this remark was made. On the next morning he was brought to the Infirmary, discovering at that time the usual symptoms of fever, namely, great bodily heat, a quick pulse, the tongue white and much furred. On the next day (Monday), his fever was much increased, but the only pain of which he complained was in the left thigh and knee, which ceased before night; in the afternoon he became delirious with much watchfulness. On Tuesday the delirium was very considerable, but without any comatose tendency; the pupil of the eye much dilated, but not insensible to light. He complained but little of pain, but when closely pressed upon the subject, he pointed to his forehead. Early in the afternoon of that day he had a convulsive fit which soon went off. In the evening all his symptoms became aggravated, and he passed the night almost without sleep. On the following morning he appeared much sunk; his breathing for the first time became difficult. He was then sufficiently sensible to answer any question put to him, but soon afterwards he became insensible, and gradually declined till about two in the afternoon, when he expired."

Those who saw this boy thought that his symptoms were of cerebral origin, and "that there was effusion within the head."

The idea of there being anything the matter with the heart did not suggest itself to his attendants; and "at no period of his illness did he complain of pain in any part of the thorax, nor was there any irregularity, either in the action of the heart or pulsation of the arteries."

"It having been considered from the general character of the symptoms that the cause of death was to be sought in the head, this was the part first inspected; but after an attentive examination of the brain,

nothing further could be remarked than that the vessels were generally turgid; not more so, however, than is frequently seen when death has taken place under circumstances that lead to no suspicion of affection of the head." The abdomen was healthy. So were the lungs. "On opening the pericardium it was found to contain between four and five ounces of turbid serous fluid, with flakes of coagulable lymph floating in it. The internal surface of the membrane, both where it constituted the exterior bag, and the reflected layer upon the heart, was covered in various situations with a thin layer of lymph exhibiting a reticulated appearance. The size of the heart was natural in relation to the age of the patient. Upon cutting through its parietes the fibres were exceedingly dark-colored, almost of a black appearance. This evidently depended on the nutrient vessels being loaded with venous blood. The fibres were also very soft and loose in their texture, being easily separable, and with facility compressed between the fingers. Upon looking closely to the cut surface exposed in the section of either ventricle, numerous small collections of dark-colored pus were visible in distinct situations among the muscular fasciculi. Some of these depositions were situated deeply, near to the cavity of the ventricle, while others were more superficial, and had elevated the reflected pericardium from the heart. The muscular fibres of the auricles were also softened in their texture, and loaded with blood, but without any collections of pus between them. All the cavities of the heart were loaded with coagulated blood. The internal lining, valves, and every other part of the organ exhibited nothing worthy of remark, except the state of general turgescence in the capillary vessels, which had also extended to the lower part of the trachea, bronchi, etc."

This case serves well to show that we may have inflammation of the muscles of the heart, sufficiently severe to give rise to suppuration, and to prove fatal in a few days, without a single symptom to call special attention to that organ.

The mistake which is most likely to be made in cases of myocarditis characterized by marked head symptoms, is that which actually was made in Mr. Stanley's case. The symptoms are apt to be attributed to cerebral, rather than to cardiac, mischief.

Such a mistake might prove a serious one to the sufferer, for the treatment appropriate to cerebral rheumatism might prove injurious in

a case of myocarditis. It is, therefore, of importance that they should not be mistaken for each other.

The points of distinction are as follows:—

In cerebral rheumatism.	*In acute myocarditis with prominent head symptoms.*
1. The temperature generally rises to 105° or more.	1. The temperature is seldom above 104°.
2. The pulse is very quick, but of fair strength, and regular.	2. The pulse is quick, but feeble; and may be irregular or intermitting.
3. The breathing is quickened, but not, as a rule, embarrassed.	3. The breathing is quickened, and is generally more or less embarrassed. There may even be orthopnœa towards the end.
4. The face is flushed; the eyes are redly injected; and the lips are generally natural in color.	4. The face is pale or dusky; the eyes are not injected; and the lips are paler than natural, or bluish in color.
5. The heart's sounds are distinct, and the impulse fair.	5. The heart's sounds are indistinct, and the pulse less than natural.
6. Death is threatened by coma.	6. Death is threatened by asthenia.

Acute myocarditis may terminate in the formation of numerous small abscesses, of one larger abscess, or in general softening of the muscular substance, without suppuration.

As a result of suppurative change, ulcers may form on the endocardial, and it is said also on the pericardial, surface. Softening, if it do not prove fatal, may result in weakening, and subsequent dilatation, of a portion of the ventricular wall; leading to the formation of cardiac aneurism, and maybe ultimately to death by rupture of the weakened portion. In very acute cases recovery is scarcely to be looked for.

Subacute myocarditis occurs in the course of acute and subacute rheumatism. Its existence is not generally recognized. I believe it to be of not uncommon occurrence. But so slight are the symptoms and physical signs to which it gives rise, that it may very readily be overlooked. It may exist either in connection with, or independently of, inflammation of the membranes.

When there is a coexistent endo- or peri-carditis, the symptoms and physical signs of this attract undivided attention, and the existence of myocarditis may not even be suspected. Its non-recognition is then not of so much practical importance; for attention is already directed to

the heart by the membranous inflammation, and any signs of feeble or failing action to which the myocarditis may give rise, though not attributed to that agency, are met by appropriate treatment.

It is when there are no signs of membranous inflammation that its recognition becomes a matter of consequence. For though by no means so formidable an ailment as the acute form of the disease, it is one which cannot with safety be ignored.

The signs of its existence are so indistinct and obscure, and so apt to escape observation, that the disease, though recognized in the *post-mortem* room, has hitherto been looked upon as unrecognizable during life. It is not always so. There are cases in which it can be diagnosed. How is the diagnosis made?

Of subjective symptoms there are practically none. Sometimes, indeed, in the more marked forms of the malady, the patient may feel less well, or have a sense of weakness without any apparent reason to account for it, but, as a rule, his sole complaint is of the pain in the joints; and there is nothing, either in his appearance or symptoms, to draw attention to the heart. On examining that organ, as one always does in the course of a rheumatic attack, there is heard no abnormal *bruit*—nothing but the systolic and diastolic sounds, succeeding each other with normal rhythm.

It is in the character of the sounds that lies the diagnostic sign of myocarditis. On careful examination they are found to lack their natural pitch. They are quite audible; but they want the clear tone of health—they are muffled and indistinct.

The character of the sounds here referred to, is not the mere feebleness which is noted in simple debility of the cardiac walls. It more resembles the alteration which is found in connection with hypertrophy. In that condition the ventricular walls are thickened, and their muscular substance increased. But, notwithstanding the greater force of the systole, the first sound at the apex is less clear than normal—it is "dull, muffled, prolonged."[1]

It is a somewhat similar muffling which characterizes myocarditis.

In this condition there is also increased thickness of the ventricular walls, the result of inflammatory swelling, effusion into, and congestion

[1] Walshe, op. cit.

of, their substance. But that which produces the thickening in myocarditis, gives rise, not to increased, but diminished, force of the systole; and this it is which makes the peculiarity of the muffling that accompanies it. The muffling of hypertrophy is accompanied by a sense of force, which is wanting in that of myocarditis.

There can be little doubt that in the thickened condition of the ventricular walls we have the explanation of this peculiar character of the heart's sounds. For the only morbid changes in connection with which it is noted, are also the only ones in which the walls are thickened. In further support of this view it is to be observed that the opposite condition of the ventricular walls, thinning and dilatation, is characterized by an opposite condition of the heart's sounds—unusual clearness.

Muffling of the heart's sounds is not peculiar to myocarditis. But muffling of the heart's sounds *arising in the course of acute or subacute rheumatism,* is diagnostic of inflammatory thickening of the ventricular walls.

When there is coincident inflammation of the membranes, this character of the sounds may be lost, if the membranous affection is at all marked.

The change is one which may very readily be overlooked, and, as a matter of fact, is constantly overlooked. The heart is daily and carefully examined in every case of acute and subacute rheumatism. But what we are intent on finding out, when we make this examination, is whether or not there is any evidence of endocarditis or pericarditis. These are the only forms of rheumatic inflammation of the heart which we recognize, or look for, at the bed-side. We acknowledge the existence of myocarditis in the *post-mortem* room; but we do not acknowledge, either its occurrence independently of inflammation of the membranes, or the possibility of diagnosing it during life. We, therefore, do not look for it. If the membranes are not inflamed, we conclude that the heart is all right.

It is a common thing after an examination of the heart to hear the remark made:—"The sounds are rather indistinct, but there is no *bruit*, no sign of any inflammatory mischief." The very indistinctness to which reference is made, is probably the result of such mischief affecting the walls of the ventricle. There must be a cause for it. If it is

of recent origin, and if there is nothing else to account for it, it is probably due to inflammatory change in the muscular walls.

In certain enfeebled conditions of system there may be a natural indistinctness of the heart's sounds. But apart from this, and apart from pericardial effusion, such indistinctness does not arise in the early part of an attack of acute or subacute rheumatism, except as a result of inflammatory thickening of the ventricular walls. If the sounds are indistinct on the first occasion on which the heart is examined, we may be unable perfectly to satisfy ourselves whether this condition is due to natural debility, or to inflammatory change. But if such indistinctness arise in the course of the case, especially if it be developed early in its course, and quickly; and if the sounds be muffled rather than feeble —a distinction which the practised ear will at once recognize and appreciate,—then we may be quite sure that the walls of the ventricle are inflamed, and that we have to do with a case of myocarditis.

How important it is that we should recognize the existence of rheumatic myocarditis occurring both in connection with, and independently of, inflammation of the membranes, will be seen when the question of treatment is discussed.

By various observers attention has been directed to the occasional occurrence of sudden death in acute rheumatism. It is probable that the explanation of this result is to be found in inflammatory softening of the ventricular walls. It certainly was so in the following case.

Case III.—A girl, aged 20, who had previously enjoyed good health, suffered from an attack of acute rheumatism in March, 1872. The attack was an ordinary one of medium severity, presenting no unusual feature, but complicated by a slight attack of endocarditis which gave rise to no subjective symptom; and the only sign of whose existence was a soft and short systolic blow at the apex. She was treated with acetate of potass, ten grains every three hours.

The endocardial blow persisted, but the rheumatic symptoms had diminished in severity by the end of the second week. On the 17th day of her illness she got up of her own accord. Her sister, who was in the room, stated that her feet had scarcely touched the floor, when she fell back on her bed, and lay there motionless. She never moved, or gave any sign of life. I saw her twenty minutes later, quite dead.

A few minutes before making the effort, she expressed herself as feeling very well, and free from pain.

On *post-mortem* examination, the mitral valve was found to be somewhat thickened, and on its auricular surface was a line of lymphy deposit. The heart's substance, especially that of the left ventricular walls, was rather dark in color, and softer than natural. On firm pressure, it broke down under the finger. On microscopic examination, the normal striæ were wanting in distinctness; and here and there the fibres had a granular aspect. There was a little effusion into the pericardium. There was no ulceration of the endocardial surface; no appearance of embolism; nothing to explain the fatal result, except the altered condition of the ventricular walls. The cranial and abdominal contents were normal.

In this case, endocarditis was diagnosed during life, and with that diagnosis I was satisfied. It did not occur to me that the muscular substance of the heart might be involved; for up to that time I had not regarded myocarditis as of more than pathological interest. The case of this girl, however, made a great impression on me. Since it occurred, I have examined into the condition of the muscular substance of the heart in every case of acute and subacute rheumatism, with as much care and attention as I have devoted to ascertaining that of the endocardium and pericardium; and have satisfied myself that the recognition of myocarditis during life is not the impossible thing that it is usually supposed to be.

The two following cases illustrate the change in the heart's sounds which is believed to result from, and be indicative of, inflammatory thickening and softening of the walls of the left ventricle, in its subacute or latent form.

Case IV.—A man, aged 44, had an attack of rheumatic fever in November, 1874. He had a similar illness in 1866. Was then confined to bed for eight weeks; but made a perfect recovery. His second attack commenced with shivering, *malaise*, and pain in the joints. He was first seen on the third day of it, the 24th of November.

November 24th. Has anxious, pained expression. Lies on his back unable to move, the least effort to do so causing intense pain. Skin covered with acid perspiration; tongue moist and furred; bowels moved

by medicine; urine scanty and high-colored; pulse 120, small and regular, temperature 101.8°; *heart's sounds normal.* To have twenty grains of acetate of potass every four hours, and ten grains of Dover's powder at bedtime. Food to consist of milk, beef tea, and light puddings.

25*th.* Passed an almost sleepless night; general state unchanged. Has great pain in the joints of knees, ankles, wrists, and fingers, which are all swollen; cannot move. Pulse 120, feeble; temperature 103°; *heart's sounds muffled in character and wanting in clearness; no bruit.* Continue treatment.

26*th.* Had an hour's troubled sleep after the Dover's powder. General condition unchanged; lies on his back quite unable to move; profuse acid perspiration; pulse 120, feeble, regular; temperature 102.8°; heart's sounds indistinct and muffled; no *bruit:* cardiac dulness normal. Omit potass and Dover's powder. To have twelve grains of salicin every three hours.

27*th.* Had a better night, sleeping in snatches; looks better, and says he feels so; joints less swollen and tender; skin covered with acid perspiration; pulse 100, of better volume, soft and compressible; temperature 99.6°; heart's sounds still somewhat muffled. Continue salicin.

28*th.* Had a pretty good night; pain nearly gone, but still felt on movement; large joints almost natural in size; those of fingers still swollen; pulse 84, of good volume and character; temperature 98.5°; heart's sounds have lost their muffled character, and are now distinct and normal, though not loud.

Patient made a good convalescence and remained well.

Case V.—A girl, aged 19, who had previously enjoyed perfect health, was laid up with an attack of acute rheumatism in May, 1878. The symptoms of the disease were all well marked.

May 10*th.* Two days ago felt out of sorts; was cold; and had aching in limbs. Yesterday the knees and ankles became very painful. Now she is in bed, the knees and ankles are slightly swollen and very tender; pulse 116°; temperature 101.2°; tongue furred; skin moist, perspiration acid; urine scanty, and high-colored. There is a slight short and soft systolic blow at the apex: cardiac dulness and impulse normal. Has no pain or uneasiness in chest. To have twenty grains

of salicin every hour for six hours, and then twenty grains every two hours.

11*th*. Has had twelve powders, equal to 240 grains of salicin. Feels better; pain and swelling of joints is less; pulse 84; temperature 99°; skin covered with acid perspiration. There is a distinct soft systolic blow at the apex; and the first sound is muffled in character; cardiac dulness normal. Continue salicin, twenty grains every two hours.

12*th*. Had a good night; feels quite well; no pain; perspiration still acid. Systolic blow unchanged; first sound still indistinct and muffled. Continue salicin, twenty grains every four hours.

14*th*. Was not seen on 13th. Feels quite well, and wishes to get up. The *bruit* at apex remains, but the first sound has lost its muffled character, and has now more the tone of health.

To take twenty grains of salicin three times a day; to have good food, and to remain in bed for a week.

In these two cases we have instances of muffling of the first sound of the heart, arising in the course of acute rheumatism. It will be seen that in each, this character of the systole was developed after the patient came under notice; and disappeared soon after the cessation of the joint symptoms and febrile disturbance.

That this change in the heart's sounds resulted from the action of the rheumatic poison, there can be no reasonable doubt; it appeared soon after its action on the system had declared itself, and disappeared soon after the usual evidence of that action had ceased.

The only recognized cause of muffling of the cardiac systole, is thickening of the ventricular walls. Such transient muffling as existed in these cases, must have been caused by a quickly produced and temporary increase in the thickness of the walls of the ventricle. It must have been quickly produced, because the muffling was quickly developed; it must have been temporary, because the muffling lasted only a few days. The only possible cause of such a temporary change in the muscular walls of the heart, is inflammatory thickening and softening, such as was noted after death in Case III.

The circumstances under which the change in the heart's sounds occurred in Cases IV. and V., *i.e.*, during an attack of acute rheumatism, are also those under which such a change in the walls, if it ever occur, is most likely to be developed.

From whichever point we approach the subject, the conclusion is forced upon us, that the change in the cardiac sounds noted in these two cases, resulted from rheumatic inflammation of the walls of the left ventricle.

With such an instance as Case III. before us, it cannot be said that the diagnosis of this condition may not be a matter of supreme importance to the patient.

CHAPTER XV.

THE TREATMENT OF LOCO-MOTOR RHEUMATISM.

If the pathology of rheumatism has been unsatisfactory, its treatment has been not less so. There is probably no disease in which so many different modes of treatment have been had recourse to. There is none in which medicinal treatment has, until very recently, more completely failed to shorten the duration of the malady.

The special mode of treatment in vogue at a given time, has generally depended on the views held regarding the nature and mode of production of rheumatism.

During the last century, and the first half of this, rheumatism was regarded as a "phlegmasia"—as an inflammation dependent, like other inflammatory affections, on exposure to cold; and differing from them only in the nature of the textures involved.

The treatment of inflammation was, at that time, essentially antiphlogistic, and consisted in the adoption of various means of depletion. The chief of these was bleeding.

Sydenham, the father of English medicine, wrote in 1666 that "the cure of rheumatism is to be sought by blood-letting." His rule was to take ten ounces of blood as soon as he saw the patient, to repeat the operation the following day, to do it again in a day or two, and, for the fourth and generally the last time, three or four days later.

But he was not satisfied with the results of this practice; for in 1679, ten years before his death, he says in a letter to Dr. Brady, "I, like yourself, have lamented that rheumatism cannot be cured without great and repeated losses of blood. This weakens the patient at the time; and if he have been previously weak, makes him more liable to other diseases for some years. . . . Reflecting upon this, I judged it likely that diet, simple, cool and nutritious, might do the work of repeated bleedings, and saving the discomforts arising therefrom. Hence I gave my patients whey instead of bleeding them." He gives the particulars of a case treated dietetically, in which the patient "recovered his full

strength, escaping all such discomforts as ten years before a similar attack, which I treated by bleeding, had entailed upon him."

Cullen, though he regarded blood-letting as "the chief remedy of acute rheumatism," and taught that "large and repeated bleedings during the first few days of the disease seem to be necessary," was careful to add that "to this some bounds are to be set; for very profuse bleedings occasion a slow recovery, and if not absolutely effectual, are ready to produce a chronic rheumatism."

Though the indiscriminate use of the lancet was condemned by other able observers, such as Heberden, Fowler, Latham, etc., bleeding continued, till well on in this century, to be the sheet-anchor in the treatment of acute rheumatism.

"In undertaking the treatment of acute or subacute rheumatism, whether we view the inflammatory state of the aponeurotic membranes as primary and idiopathic, or secondary and symptomatic, it is necessary in the first instance to adopt the antiphlogistic method of treatment, and to carry it on with some degree of energy, and to a considerable extent.

"The different branches of the antiphlogistic regimen requisite in the treatment of rheumatism are blood-letting, general and local, the occasional employment of cathartics, the occasional employment of emetics, especially tartar emetic, the use of diaphoretics, and the use of revellents. . . .

"*First.* General blood-letting, in order to be beneficial, ought to be performed early in the disease, and carried to a considerable extent. . . . It should be carried at first to twenty or twenty-five or thirty ounces at once if possible; and within twenty-four hours to as much more.

"*Secondly.* The influence of general blood-letting must be aided by the conjoined operation of various adjuvants. Full vomiting produced by ipecacuanha and antimony is in the majority of cases requisite; and complete evacuation of the bowels by eccoprotics and even cathartics is quite indispensable.

"*Thirdly.* It is of the utmost importance, in attempting the thorough removal of rheumatic pains, to conjoin with blood-letting, or after its use, the administration of full doses of tartrate of antimony.

"*Fourthly.* It is of great moment, if the bowels have been previ-

ously well opened, to exhibit, after the first blood-letting, an opiate of forty or fifty minims of the solution of muriate of morphia; or if the bowels have not been freely moved, to effect this indication, and take a second blood-letting, and after this to administer the opiate, which may be either given alone or conjoined with antimony."[1]

So wrote Dr. Craigie in 1840.

In that year appeared also Bouillaud's "Traité Clinique du Rhumatisme Articulaire," in which the treatment by bleeding *coup sur coup* was advocated with characteristic ability and energy.

To Bouillaud, indeed, belongs the credit of having systematized this mode of treatment. The full extent of his credit in this respect is not generally recognized. Previous to his time there was little or no method in the practice of phlebotomy. To take so many ounces of blood, and to repeat the operation in one, two, or more days, was all the recommendation. Bouillaud insisted that there should not be too long an interval between the different bleedings—that the second should be had recourse to before the effects of the first had fully passed off, and the third before the benefit of the second was lost. That is what he meant by his recommendation to bleed *coup sur coup*. It was the frequent repetition of the operation, rather than the quantity of blood taken, which formed the characteristic feature of his mode of treatment.

If the pathological views which then prevailed were correct, and if bleeding were the important therapeutic agent which it was believed to be, there can be no doubt that Bouillaud's idea was therapeutically sound. No single dose of any remedy could stop a disease like acute rheumatism. It would have to be repeated from time to time; and to get its full beneficial effects the second dose should be given before the first had quite ceased to act. Bouillaud's merit consists in having applied this sound therapeutic rule to the practice of phlebotomy.

The use of the lancet implied also the adoption of other antiphlogistic measures, low diet, purgatives, diaphoretics, etc.

About the middle of this century the practice of phlebotomy, and the pathological views on which it was founded, were vigorously assailed. Facts tended to show that patients recovered more quickly and satisfac-

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[1] Elements of the Practice of Physic, by David Craigie, M.D., F.R.S.E., Vol. II. 1840.

torily when they were not bled, than when they were. This was noted in acute rheumatism, as in other acute diseases. The rapid accumulation of such facts produced a marked reaction against the old mode of treatment; and within twenty years of the time that Bouillaud's book appeared, the practice of bleeding in acute rheumatism was all but abandoned.

Other remedies besides bleeding were used to allay the inflammation.

Purgatives were at one time a good deal used. Those most in vogue were the saline, chiefly the sulphates of magnesia and soda. Calomel was also thus employed, especially by Latham, and with results which gave satisfaction.

Diaphoretics, especially ipecacuanha and antimony in combination with opium, have been at all times much used. Dover's powder has enjoyed a specially high reputation. Referring to it, Cullen says, "Notwithstanding what I said in favor of venesection, I must own that I never saw a cure very quickly expedited by venesection alone, in the cure of any violent case of the disease; for the disease is liable to linger, and continue for a long time, and to pass into a chronic state. The Dover's powder gives us an opportunity of more effectually and more safely curing the disease than by bleeding alone."

Opium alone, except as a diaphoretic, was condemned by Cullen; but has had much said in its favor in more recent times by Corrigan, Trousseau, and others.

Cinchona, and its alkaloid quinine, have at different times had their claims to favorable consideration pressed. Morton was the first to use cinchona in acute rheumatism. Cullen gave the great weight of his authority against it. He regarded its employment as "absolutely improper and manifestly hurtful," except in cases in which the acute stage had been subdued by bleeding and other measures, and in which the ailment threatened to become periodic. Haygarth,[1] who first used it on the recommendation of Dr. Fothergill, brought forward much testimony in its favor. George Fordyce[2] used it early and freely.

Its alkaloid quinine was at one time freely used, especially in France. A suspicion that it gave rise to cerebral symptoms and dangers pre-

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[1] Clinical History of Diseases, Part I. 1805.
[2] Elements of the Practice of Physic. 1791.

vented many from trying it, notwithstanding the strong recommendations of Briquet, Monneret, and others.

Garrod [1] has tried to revive this treatment in a modified form. He gives the quinine along with carbonate of potass—five grains of the former and thirty grains of the latter, every four hours "until the joint affection and febrile disturbance have completely abated." The benefits which he claims for this plan are its greater efficacy, a diminished tendency to relapse, and a more satisfactory convalescence.

Colchicum has been much used in the treatment of rheumatism; but there is no valid evidence of its exercising any beneficial action. Garrod, who regards its power to subdue gouty inflammation as beyond doubt, says that "it possesses no influence in checking the progress of rheumatic fever." To give relief to the pain of rheumatism it requires to be given in quantity large enough to cause depression of the heart's action; and that is a condition which cannot safely be induced in the course of an ailment which tends specially to affect the heart.

Guaiacum has long enjoyed considerable reputation as a remedy in rheumatism. Originally introduced by Dr. Dawson, it found its chief advocate in Fuller, who regarded it as useful in all stages of the disease. It is nowadays prescribed chiefly in the chronic form. Any good effects which it produces are probably due to its stimulant action on the skin.

Nitrate of potass was at one time a good deal used as a diuretic and refrigerant in febrile ailments. Brocklesby recommended it in acute rheumatism. He gave as much as two drachms dissolved in some diluent three, four, or five times a day. Given thus, there was got both a diaphoretic and diuretic action.

This treatment was revived by Dr. Basham, who not only gave the nitre internally, but also applied it locally to the inflamed joints. The results of this treatment seem to have been as good as those of any other.

Other remedies, aconite, veratrine, digitalis, actæa racemosa, etc., have enjoyed a passing reputation, and had their claims advocated by different observers. But not one of them has stood the tests of time and investigation.

About the time that bleeding went out of fashion, new views began to be entertained regarding the pathology of rheumatism. This was all

[1] Reynolds' System of Medicine, article "Rheumatism," Vol. I. 1866.

but inevitable. If bleeding was wrong, the pathological view on which that treatment was founded was also likely to be erroneous. If to take blood not only did no good, but even did positive harm, then were there grave reasons for questioning the soundness of what was generally believed regarding the nature of rheumatism. Doubts were started, investigation was stimulated, the symptoms of the malady were subjected to fresh scrutiny, the opinions of the older writers were regarded with a healthy scepticism, and by-and-by new views began to be ventilated.

The question began to be discussed whether rheumatic inflammation was not altogether peculiar, and due to some special poison circulating in the blood, rather than to the operation of any external agency.

The acid condition of the secretions attracted early and prominent attention, and was regarded as a possible cause of the rheumatism. Prout made the definite suggestion that lactic acid was the rheumatic poison. Ably advocated by Todd, Fuller, and others, this view was soon generally accepted, at least in this country.

Altered views of causation led to altered treatment. If lactic acid were the rheumatic poison, it was plain that the proper treatment was to promote its elimination, and to counteract its effects.

It is probable that the *materies morbi* in rheumatic fever is lactic acid or some analogous agent. We know that the natural emunctory of this is the skin. Many chemists maintain that it will also escape by the kidneys; and if it ever does so, perhaps this is more likely during rheumatic fever than at any other time.

Again, since vitiated digestion is apt to produce it in undue quantity, and it, therefore, is formed abundantly in the stomach, there is every reason to think a certain proportion of it may be carried off through the alimentary canal. The indications are, then, to promote the action of the skin, the kidneys, and the bowels; to use antacid remedies; and to give large quantities of fluid for the free dilution of the *materies morbi*, and to supply the waste caused by the drainage from diaphoresis and diuresis."[1]

The acid theory naturally led to alkaline treatment, and that has continued till very recently to be *the* treatment for rheumatism. "If the *materies morbi* be indeed an acid or an acidulous compound—if it be

[1] Todd's Clinical Lectures, p. 69.

lactic acid, for instance, as there are cogent reasons for believing it to be,—then will its neutralization be effected, its irritative property probably diminished, and its elimination promoted, by a free exhibition of alkalies and neutral salts."[1]

The alkaline salts chiefly used have been the bicarbonate and acetate of potass, given in the dose of fifteen to thirty grains every three or four hours. The evidence adduced by Fuller, Garrod, Basham, and others in support of this treatment, is sufficient to demonstrate its superiority over any which preceded it. But the sanguine anticipations of its earlier advocates have not been realized; for it has been found in practice that alkalies may be given so as to render the urine alkaline, without diminishing the joint pain or allaying the fever.

As time advanced, and facts accumulated, it became evident that the alkaline treatment did not materially shorten the natural duration of acute rheumatism, or decidedly diminish the tendency to heart complications—the two advantages which have been specially claimed for it.

We have already seen that the theory on which that treatment is based is untenable; and that the rheumatic poison is not lactic acid, but in all probability a poison introduced from without.

The theory on which the alkaline treatment was founded, being erroneous, we are not surprised to find that treatment fail to produce the good results which its early advocates anticipated. But though it has failed to do all that was hoped from it, there can be no doubt that in some cases the administration of alkalies is undoubtedly beneficial, as will be explained hereafter.

Impressed with a sense of the failure of this mode of treatment, physicians looked about for something better. Owen Rees used lemon-juice, and got from it results which were at least as good as those which followed the administration of alkalies.

Some gave up all medicinal treatment, and simply kept the patient warm in bed, gave him light simple diet, and administered some *placebo*.

Dr. Flint[2] published in 1863 an account of thirteen cases treated on this plan with good results.

Two years later an equally good report was given by Dr. Sutton,[3] of

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[1] Fuller On Rheumatism, p. 77.

[2] American Journal of the Medical Sciences, July, 1863.

[3] Guy's Hospital Reports, 1865.

forty-one cases treated in Guy's Hospital, and which got medicinally only mint water.

This expectant plan of treatment was adopted by many, with results as satisfactory as those got from more active measures.

"I am quite certain," says Dr. Garrod, "that many cases, even of severe rheumatic fever, get rapidly well without the administration of drugs; and on simple colored or camphor water the improvement is often so quick and satisfactory that, had not the nature of the treatment been known, great virtue would surely have been ascribed to it."

This expectant plan of treatment is really that which was recommended and practised by Sydenham in the later part of his career. To treat a patient by mint water, is practically the same as treating him by whey, which Sydenham did two hundred years ago.

It is curious to find the leading physicians of the nineteenth century going back to the same plan of treatment which was recommended by the father of English medicine in the seventeenth.

Dr. Russell Reynolds, dissatisfied with the alkaline treatment, tried in acute rheumatism a remedy which had proved serviceable in some forms of spreading inflammation, the tincture of muriate of iron. His results were as good as those got by any other treatment; though his cases are too few to be of statistical value.

Dr. Herbert Davies, reviving an old practice, had recourse to free blistering of the inflamed joints, with very satisfactory results.

Such are the chief remedial measures which have been adopted in the treatment of acute rheumatism. Antiphlogistic treatment, the alkaline treatment, and the expectant treatment, are the only ones which have met with anything like general approval.

Antiphlogistic treatment was practised, not because of the proved excellence of its results—for two hundred years ago these were regarded as unsatisfactory by Sydenham, and have frequently since then been called in question by others,—but because such treatment was the legitimate outcome of the views held regarding the nature and mode of production of rheumatism.

The alkaline treatment was adopted, not because it had been proved to be specially beneficial, but because such treatment was a therapeutic sequence of the generally accepted acid theory.

The expectant treatment was the practical expression of the opinion which had gradually been gaining ground, that the results of the alkaline treatment were not satisfactory. It succeeded the failure of the alkaline treatment in the nineteenth century, just as in the hands of Sydenham it succeeded the acknowledged failure of the antiphlogistic treatment in the seventeenth.

Adopting the pathological views advocated in these pages; regarding the rheumatic poison as an organism which is propagated in the system, and the extent of this propagation as dependent on the quantity of the second factor which naturally exists there, we have no difficulty in explaining both the occasional successes, and ultimate general failure, of every plan of treatment to which reference has been made.

If this theory be correct, it is evident that, no matter what the treatment adopted, cases must occur in which the attack will be short, and quickly got over, because the system of the sufferer contains little of the second factor requisite to the propagation and action of the rheumatic poison. Such cases would get quickly well under any treatment, or no treatment.

It is equally evident, on this theory, that no plan of treatment hitherto adopted could materially curtail the duration of the disease in one in whom the rheumatic constitution was very marked, and in whom the second factor existed in large quantity, and was speedily reproduced. In such a one the disease would be prolonged and tedious under any of the old forms of treatment; for not one of them could prevent, or even check, the action of such a substance as, on this theory, the rheumatic poison is believed to be.

Quinine is the only remedy hitherto used which seemed to hold out a prospect of success; and it had already been well tried without any marked result.

But the fact that it exercises a specific action on the disease to which we have seen that rheumatism is most nearly allied, was to be accepted as a hopeful indication that there might be found a remedy capable of counteracting the effect of the rheumatic poison, in the same way that quinine does that of ague.

In connection with the action of quinine on the various forms of intermittent and remittent fever, and indeed in connection with the

action of the Cinchonaceæ generally on the diseases of tropical climates (ipecacuanha in dysentery, for instance) one fact had always strongly impressed me—that the maladies on whose course they exercise the most beneficial action are most prevalent in those countries in which the Cinchonaceæ grow most readily,—nature seeming to produce the remedy under climatic conditions similar to those which give rise to the disease.

Impressed with this fact, and believing in the miasmatic origin of rheumatism, it seemed to me that a remedy for that disease was most hopefully to be looked for among those plants and trees whose favorite habitat presented conditions analogous to those under which the rheumatic miasm seemed most to prevail.

A low-lying damp locality, with a cold rather than warm climate, are the conditions under which rheumatism is most likely to arise.

On reflection, it seemed to me that the plants whose haunts best corresponded to this description, were those belonging to the natural order Salicaceæ—the various forms of willow. Among the Salicaceæ, therefore, I determined to search for a remedy for rheumatism.

The bark of many species of willow contains a bitter principle called salicin. This principle was exactly what I wanted. To it, therefore, I determined to have recourse.

I began to use salicin in the treatment of rheumatism in November, 1874. A short experience of it sufficed to show that my expectations were likely to be more than realized.

In March, 1876, I published[1] some account of my experience up to that date. What I then said was as follows:—

"From so small an experience of salicin as I have had, I would not assert in anything like a dogmatic manner the full extent of its usefulness. I would simply indicate the following conclusions as those to which I have been led, and which, I hope, a more extended experience of its use may confirm.

"1. We have in salicin a valuable remedy in the treatment of acute rheumatism.

"2. The more acute the case, the more marked the benefit produced.

"3. In acute cases its beneficial action is generally apparent within

[1] Lancet, March 4 and 11, 1876.

twenty-four, always within forty-eight, hours of its administration in sufficient dose.

"4. Given thus at the commencement of the attack, it seems sometimes to arrest the course of the malady as effectively as quinine cures an ague, or ipecacuanha a dysentery.

"5. Relief of pain is always one of the earliest effects produced.

"6. In acute cases, relief of pain and a fall of temperature generally occur simultaneously.

"7. In subacute cases the pain is sometimes decidedly relieved before the temperature begins to fall; this is especially the case when, as is frequently observed in those of nervous temperament, the pain is proportionally greater than the abnormal rise of temperature.

"8. In chronic rheumatism, salicin sometimes does good where other remedies fail; but it also sometimes fails where others do good."

Subsequent experience, and more extended observation, have necessarily led to a fuller knowledge of the therapeutic uses of the drug; but they have not led me to recall, or even to modify, any of these conclusions. And not only have they been confirmed by my own subsequent experience—they have also been very generally endorsed by the profession.

While these observations on salicin were being made, Kolbe, having discovered a method of manufacturing salicylic acid (originally prepared from salicin) from carbolic acid, was bent on finding some use for it. First tried by surgeons as an antiseptic, it was also freely experimented with by physicians in all sorts of diseases, but chiefly in those attended by fever. Its febrifuge properties were soon recognized, and much that was favorable hoped from, and reported of, its action in typhoid fever, diphtheria, erysipelas, pyæmia, etc. But it was soon seen that the disease in which it did most good was acute rheumatism.

Early in 1876, Stricker[1] and Riess[2] published a most favorable account of their experience of its employment in that disease. Their results were quite in accordance with those which I had got from salicin.

The conclusions at which he had arrived are thus formulated by Stricker:[3]—

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[1] Berliner Klinische Wochenschrift, Nos. 1 and 2, 1876.

[2] Ibid., No. 7, 1876.

[3] Ibid., February 21, 1876; and London Medical Record, June 15, 1876.

1. Salicylic acid appears to be a rapid and radical remedy in recent cases of genuine acute rheumatism of the joints.

2. It is not injurious to the human organism when administered every hour in doses varying from 7½ to 15 grains.

3. It can be given in these doses for a longer time to young and strong individuals than to the old and feeble.

4. In the latter, it produces toxic symptoms more readily than in the former.

5. The toxic symptoms vary in degree.

6. Those most commonly met with are noises in the ears, difficulty of hearing, and diaphoresis; when these occur the administration of the medicine should be discontinued.

7. If salicylic acid be found to fully answer the expectations entertained regarding it, the internal administration of a certain quantity may be expected to prevent the occurrence of fresh attacks in hitherto unaffected joints, and also secondary inflammation of serous membranes, especially the endocardium.

8. To prevent relapse, the medicine must be continued in smaller doses for some days after the termination of the main treatment.

9. Salicylic acid is of doubtful utility in chronic articular rheumatism.

10. It is not likely to be of use in gonorrhœal or diarrhœal rheumatism, or in the polyarthritis attending septicæmia.

Previous to the publication of the German reports, I had myself, while making my observations on salicin, tried salicylic acid in a case of subacute rheumatism. It did good to the rheumatism, but caused so much irritation of the throat and stomach that it was omitted, and salicin given instead. I did not again have recourse to it, till its use had become general.

Results so striking as those got by the German observers from salicylic acid, and by myself from salicin, could not fail to attract general attention. Observations were made on all hands. The journals in England, France, Germany, and America contained numerous reports of cases of rheumatism treated by these drugs; and it soon became evident that the statements of the original observers were, in the main, correct.

The favorable experience of Stricker and Riess is endorsed by German physicians generally.

In France it has been equally successful. M. Sée tells us that by this treatment he cures acute rheumatism in from two to four days.

In America, Dr. Brown[1] found that from the commencement of treatment to the cessation of pain, the average time was 2.85 days. Dessau[2] found that the majority of his patients could return to their avocations in a week; and thinks that the new treatment is destined to supersede all others.

In this country, the results have been equally good; and from all parts of it have come the warmest commendations of the new treatment. "There are few practitioners who have reported themselves as disappointed in the use of this drug; or, to put it at once strongly and carefully, more disappointed than in the use of quinine for ague. There has not been, in fact, such a consensus of medical opinion on any therapeutic question for many years, as on the power of this drug in one form or other to cure rheumatic fever."[3]

Though the recommendations of the original observers have been, in the main, borne out by the experience of others, there have been reported cases which proved fatal by hyperpyrexia, or by cardiac complications, notwithstanding the free administration of salicin or salicylic acid.

But no one ever claimed for these remedies the power to rob acute rheumatism of all its dangers. In my original paper the action of salicin in acute rheumatism was compared to that of quinine in intermittent fevers, and of ipecacuanha in dysentery. We do not deny the specific effects of quinine in ague, and of ipecacuanha in dysentery, or call in question their power to arrest the course of these maladies, because they fail to cure every case.

In studying this question, it is essential that we should distinguish between the immediate and constant effects of the rheumatic poison, and the more or less accidental morbid changes which may take place in the course of the disease to which it gives rise. An anti-rheumatic remedy may exercise a powerful influence in arresting the former, without having any direct action on the latter.

It would be as unreasonable to expect the salicyl compounds to put

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[1] Boston Medical and Surgical Journal, February 8, 1877.
[2] New York Medical Record, April 7, 1877. [3] Lancet, July 8, 1877.

a stop to the cerebral and cardiac complications of acute rheumatism, as it would be to expect the cinchona compounds to prevent splenic enlargement in aguish subjects; or ipecacuanha to abolish the hepatic complications of dysentery.

The full extent of, and the exact limits to, the usefulness of the salicyl compounds in acute rheumatism, can be understood only when we have a definite idea, on the one hand, of the true nature of rheumatism, and of its characteristic morbid changes; and on the other, of the mode of action of the salicyl compounds.

The former point we have already considered. We have seen reason to regard rheumatism as a miasmatic disease, resulting from the propagation in the system of the minute organisms which constitute its poison. Its characteristic morbid lesion consists in inflammation originating in the white fibrous tissues, and frequently spreading from them to contiguous textures. The results of such a process, obviously depend on the situation and surroundings of the special portion of fibrous tissue which happens to be the seat of inflammation.

Rheumatic inflammation of the dura mater very soon gives rise to morbid changes which inevitably cause death, in spite of all treatment.

Rheumatic inflammation of the valves of the heart can scarcely exist without producing serious damage to the affected tissue—a damage, too, which is generally permanent. But rheumatic inflammation of the fibrous textures of a joint may persist for weeks without producing more than temporary inconvenience. The cause of the disturbance is the same in each. *It is no peculiarity in the morbid process, but the peculiarity of its seat,* which makes the marked difference in the results—as will be more fully explained further on.

The time has not yet, and cannot for some years come, at which a comprehensive and satisfactory statistical statement of the results of the new treatment can be compiled, and that for several reasons:—

First, the statistics are not sufficiently numerous.

Second, the proper mode of applying the treatment has not been sufficiently known and practised to make even those statistics which we have of like value; and selected statistics lack the impartiality necessary to truthful demonstration.

Third, our knowledge of the pathology of rheumatism is not sufficiently accurate to enable us to distinguish between those cases to which

the salicyl treatment is specially applicable, and those to which it is less suited.

And fourth, the difficulty is still further increased by our ignorance of the mode of action of salicin and salicylic acid.

Were I to utilize any of the statistics and cases which have been published, I should have to utilize all: otherwise I should be open to the charge of partiality, and of selecting only those which seemed favorable. Were I to utilize all, I should present for the reader's consideration a mass of cases differing so much in nature, and in details of treatment, that useful inference would be impossible.

The objects in view are to indicate (1) the cases to which the salicyl treatment is, and those to which it is not, suitable; and (2) the manner in which that treatment should be applied. These objects will be better attained by a judicious selection of cases, successful and unsuccessful, than by giving statistics in which all cases, no matter how different, are slumped together under the one common denomination—Rheumatism; and in which all who took salicin or salicylic acid are regarded as having been treated alike, no matter how different the dose, or how varied the mode of administration of the remedy.

The forms of rheumatism with which we have to deal are the acute, subacute, and chronic. It is to the acute and subacute forms, *i.e.*, to rheumatic fever, that the salicyl treatment is most applicable. To get its full beneficial effects the remedy must be given in full and frequently repeated dose. The patient, of course, is confined to bed; the bowels are relieved by medicine, if necessary; and the diet is light and simple, consisting mainly of milk and farinaceæ.

The salicyl treatment should be begun as soon as possible; for, in the interest of the heart, every hour is of importance. Twenty to forty grains should be given every hour till there is decided evidence of its action. It will generally be found that before an ounce has been consumed, often before half that quantity has been taken, there is a marked improvement. Relief of pain is the first indication of this. With the continuance of the remedy, improvement progresses; and, often within twenty-four, generally within forty-eight, hours from the commencement of treatment, the pain is gone, and the temperature is at or near the normal standard.

As the symptoms decline, the dose may be diminished: but it is

well not to do this too quickly, or too early; for if the remedy be omitted too soon, or given in inadequate dose, the symptoms are apt to recur. The object in view is to keep the system persistently under the salicyl influence.

The salicyl compounds are so rapidly eliminated, that their full beneficial effects can be got only by giving them frequently, as well as in full dose. Moreover, one can never tell the time at which their curative effects have been completely produced. For this reason the salicyl treatment should be gone on with for some time after convalescence seems to be established. There is no definite time at which one can say to the patient, "Now you are all right, and may leave off your medicine without any fear of a return of your ailment." On the contrary, he should be given to understand that there is a tendency to a recurrence of the symptoms, and that the medicine must be taken for some time after all pain has ceased.

It takes about an ounce of salicin or salicylic acid to remove the acute symptoms. That quantity should be taken within the first sixteen or twenty-four hours, in doses of twenty to forty grains, at first every hour, and then every two hours, as the acute symptoms begin to decline. A second ounce should be consumed in the next forty-eight hours. After that, twenty to thirty grains may be taken every four hours, for two or three days; and for a week or ten days more, that quantity should be taken three times a day. By that time the patient will most likely be safe. Any threatening of a return of the rheumatic symptoms must be at once met by a return to large, and frequently repeated, doses of the remedy.

If salicin be the form in which it is given, it may be gone on with for some time without hesitation; for it is a good bitter tonic as well as an anti-rheumatic, and those treated by it convalesce more quickly, and pick up more rapidly, than those who take salicylic acid.

The patient should be in bed for a week. No matter how speedily the pain is relieved and the fever abolished, the affected fibrous textures cannot at once resume their normal condition: and until they have had time to do so, they should have no work to do. It is of the utmost importance that a rheumatic attack should be perfectly recovered from, for the chances are that there will be more of them. Any injury done during a first attack, is almost sure to be increased by subsequent ones.

Treated thus, the course of uncomplicated acute rheumatism is arrested, the pain is abolished, and permanent convalescence begins frequently within twenty-four, and generally within forty-eight, hours of the time that treatment commences. In first attacks, and in young subjects, such is almost invariably the course of events, when there is no cardiac complication.

How different from the duration of the disease under other methods of treatment! Under all of them it was common for the acute symptoms to last for three or four weeks; and twice that time frequently elapsed before the patient was free from pain or able to leave his bed. Now it is often difficult to keep him in bed for more than two or three days.

The following cases illustrate the good effects of the salicyl compounds:

Case VI.—Margaret T——, aged 16, nursery-maid; never had rheumatism before. Was quite well on April 12, 1876. On the 13th felt out of sorts, and had a general feeling of cold, with some pain in the limbs. On the 14th the pains increased, and towards evening got very bad. Being anxious to continue at work, she got up on the 15th and went about as usual, saying nothing to any one about her pains, which were severe in both arms and legs. On the 16th she got up, but was obliged to go back to bed. In the evening I received a note from her mistress, requesting me to see her as soon as possible, as she was afraid that the girl was dying. On arriving at the house, I was told that the girl was in bed, screaming with agony. I heard her cries before entering the room. She was not hysterical, and the screams were clearly caused by pain.

April 16th, vesp. Lies in bed unable to move, and every now and then screaming with pain. The back, shoulders, elbows, wrists, knees, and ankles are all the seat of severe pain, but the knees and ankles are most complained of. All these joints are slightly swollen, and so exquisitely tender that the least touch or movement causes her to scream. Has no pain in chest. Skin hot, not perspiring; tongue moist and furred; urine scanty, high-colored, and loaded with pink urates. Has a soft blowing murmur with first sound, loudest at apex, but audible over whole heart. Pulse 112; respiration 20; temperature 103.8°. To have fifteen grains of salicin every hour till three powders are taken, and then one every two hours.

17*th, mane.* Wandered at times during the night, but had occasional short snatches of sleep. Pain, especially in ankles and knees, is still severe, but not nearly so bad as yesterday. Can move the right leg a little, and does not complain when the joints are touched. Indeed she allows them to be pretty firmly grasped without complaining; yesterday the least touch made her scream. Tongue furred; skin moist, and perspiration acid. Urine scanty and high-colored; bowels confined. Cardiac blow is softer in character, and precedes as well as accompanies the first sound at the apex. Still heard over whole heart, but not so distinctly as yesterday. Pulse 96; respirations 26; temperature 102.8°. Has had eight powders, equal to 120 grains of salicin. To continue to take fifteen grains every two hours.

18*th, mane.* Had a good night, free from pain. To-day feels quite well. Has no pain in any of the joints, and can move the limbs without more discomfort than what is caused by a slight feeling of stiffness in the knees. Tongue cleaning; skin natural. Pulse 72, barely perceptible; respirations 20; temperature 99.6°. Heart's action irregular; murmur still soft, has lost its systolic character, and is now purely præ-systolic; distinct at apex, but scarcely audible an inch from that point. Has had eighteen powders, equal to 270 grains of salicin.

19*th.* Slept well; is free from pain, and feels quite well. Wishes to get up. Tongue clean; skin natural; bowels moved; urine abundant, of pale amber color. Pulse 70, feeble, irregular; respirations 20; temperature 98.2°. Has had in all 405 grains of salicin.

The cardiac blow remained, but gave rise to no subjective phenomena. There was no return of the rheumatism. She went on with the salicin for a fortnight.

Rapid as was the cure in this case—the pain having been practically abolished within twenty-four, and the temperature brought to the normal within, at the most, sixty hours of the time that treatment commenced—it would probably have been still more rapid had I given the salicin in the full dose in which I now administer it. At the time that Margaret T——'s case occurred (April, 1876) the remedy was still on its trial, and the present certainty regarding the safety as well as the desirability of large doses had not been attained. To such a case occurring now I would give double the dose which Margaret T—— got;

and probably with a more rapid result—as in the following case, which bore a close resemblance to hers.

Case VII.—Jane S——, aged 17; had always enjoyed good health. With the exception of measles and scarlatina in childhood, never had any ailment.

On May 26, 1878, she felt out of sorts, and had such aching in the limbs that she did not leave the house. On the following day she was worse, and towards night got very bad.

May 28th. Lies in bed, unable to move, the least effort to do so causing intense pain, and making her scream. Has anxious pained expression. The knees and wrists are most painful, but the ankles, right shoulder and neck are also complained of. The affected joints are a little swollen, and exquisitely tender; except over the wrists, there is no redness of the surface. Tongue moist and furred. Skin hot, not perspiring; bowels moved by medicine; urine scanty, and loaded with urates. Heart's sounds normal. Pulse 112; respirations 22; temperature 103°. To have thirty grains of salicin every hour till decidedly relieved.

She began to take the medicine at 6 p. m. Was then in great pain. She felt easier after the third powder; and after the fifth (taken at 10 p.m.), was so decidedly relieved that she fell asleep. Her mother, who remained beside her all night, stated that she would probably have slept on, but that she woke her up to give the salicin at eleven o'clock, and at midnight. After that, she had a powder only every second hour.

29th. Has a pleased, smiling expression. Is quite free from pain, except when joints are pressed; allows one to grasp them, and can move them without more than a feeling of stiffness. Thinks she would have slept all night if her mother had not wakened her to give the medicine. Perspired a good deal during night. Skin is now covered with acid perspiration; saliva acid; tongue cleaner; pulse 88; respirations 20; temperature 99.8°. Heart's sounds normal. Up to this time (9.30 a.m.) has taken eleven powders, equal to 330 grains of salicin. To have thirty grains every two hours.

7 p.m. Has had no pain, and says she would like to get up. Complains only of a slight degree of deafness. This her mother noticed before the patient did. Has perspired a good deal; reaction acid. The

joints feel stiff when she tries to move them, but can be firmly pressed without pain. Pulse 76; respirations 20; temperature 98°. Heart's sounds normal. Has had in all exactly one ounce of salicin, 16 thirty-grain doses.

She continued to take the salicin in gradually diminishing dose for four days, during which she was kept in bed. At the end of that time she was allowed to get up, and the salicin was given in twenty-grain doses four times a day for a week longer. She made a perfect recovery, and had no return of pain.

In this case the acute pain was abolished within six, and all joint tenderness within twenty-four, hours of the time that treatment commenced. Within that time, too, the temperature had fallen from 103° to the normal standard, a fall of five degrees.

CASE VIII.—James S——, æt. 30, a robust well-built man; had rheumatic fever for the first time four years ago. Was then two months in bed, and three off work.

December 31, 1878. Two days ago was seized with pain in right knee. Yesterday the right was a little better, but the left became very painful. To-day the right shoulder and left ankle are also affected. Of the affected joints the right knee is the only one that is swollen, and it is only slightly so; the other joints are very tender, but none of them red. Had little or no sleep last night from severity of pain. Tongue furred; bowels moved by medicine; urine high-colored, and depositing pink urates; skin moist, perspiration acid; pulse 100; respirations 22; temperature 101°. Heart normal. To have thirty grains of salicin every hour for six hours; then every two.

January 1, 1879. Felt better after four powders, and by night was so relieved that he slept well, waking up only twice—on each occasion taking a powder. Has taken altogether ten of them, equal to 300 grains of salicin. Is quite free from pain. Felt so well this morning that he got up and dressed, and at time of visit was walking about the house. Was ordered to go to bed. In bed is quite free from pain; but when walking about felt his left knee and ankle a little. Skin covered with acid perspiration; urine less scanty, of amber color, with slight deposit of urates. Heart normal. Just after getting into bed pulse was 88; respirations 20; temperature 98.8°. A powder every two hours.

He perspired very freely during the day, and in the evening felt so well that he got up again for a couple of hours.

2nd. Slept well all night. Took no powder between ten last night and seven this morning. Has had in all eighteen powders, equal to 540 grains. Perspiring freely—secretion acid; has no pain; swelling and tenderness quite gone; pulse 72; respirations 18; temperature 98.3°. He was ordered to take the salicin three times a day for ten days. He remained well, and resumed work on the 8th of January. In this case the attack was abolished within twenty-four hours.

CASE IX.—John W——, æt. 34; has twice had rheumatic fever, once at 18, and again at 24.

On each occasion was laid up for six weeks. Present illness began three days ago with *malaise* and aching in limbs. Pains have steadily got worse, and have become localized in joints.

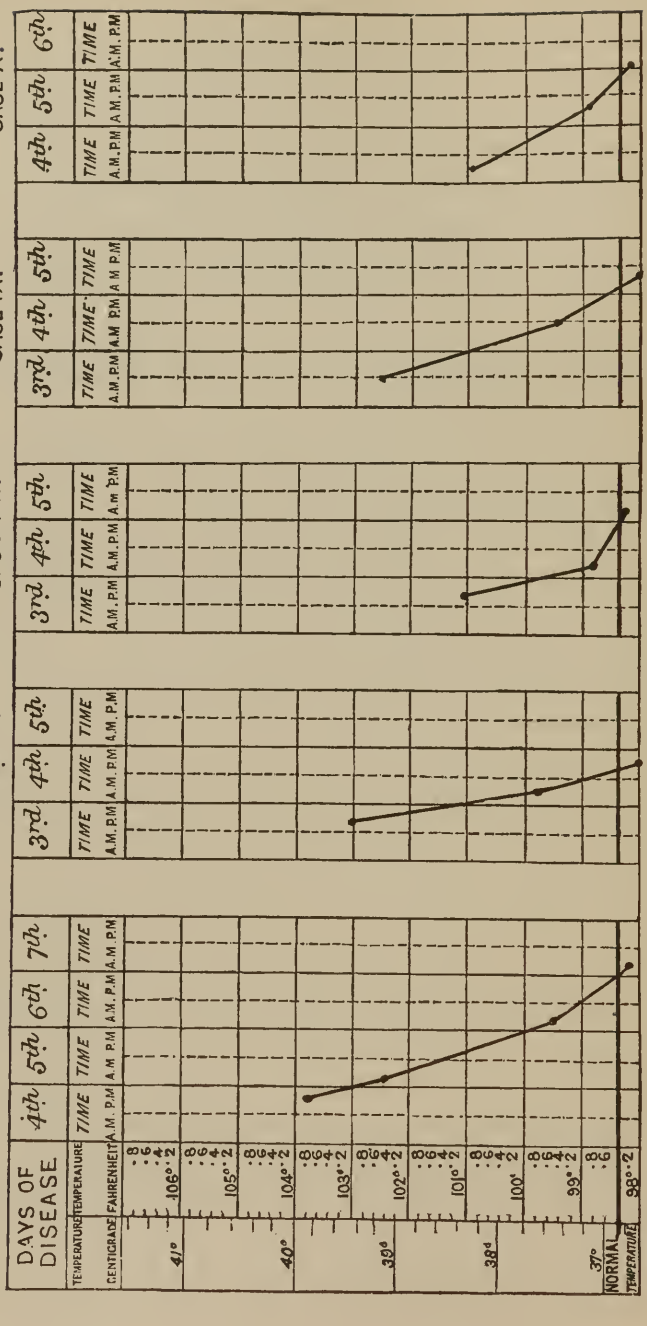
November 4, 1878. Skin hot; expression anxious; tongue furred; urine high-colored and scanty; pulse 116; respirations 24; temperature 102.5°; ankles, knees, right shoulder, and fingers of right hand are swollen and painful. The heart's sounds are normal. To take thirty grains of salicylate of soda every hour till pain is relieved; after that, every two hours.

5th. Is much better. Felt easier after the third dose of the medicine. Had a good night, but perspired a great deal. Is now covered with acid perspiration; saliva is also acid. The swelling is all but gone from the joints; and there is no pain except when they are moved or pressed. Heart normal. Pulse 92; respirations 20; temperature 99.6°. Took the medicine every hour for four hours. He was then easier, and took it every two hours. Has had in all nine doses, equal to 270 grains. Says he feels a little squeamish after it. To take a dose every three hours.

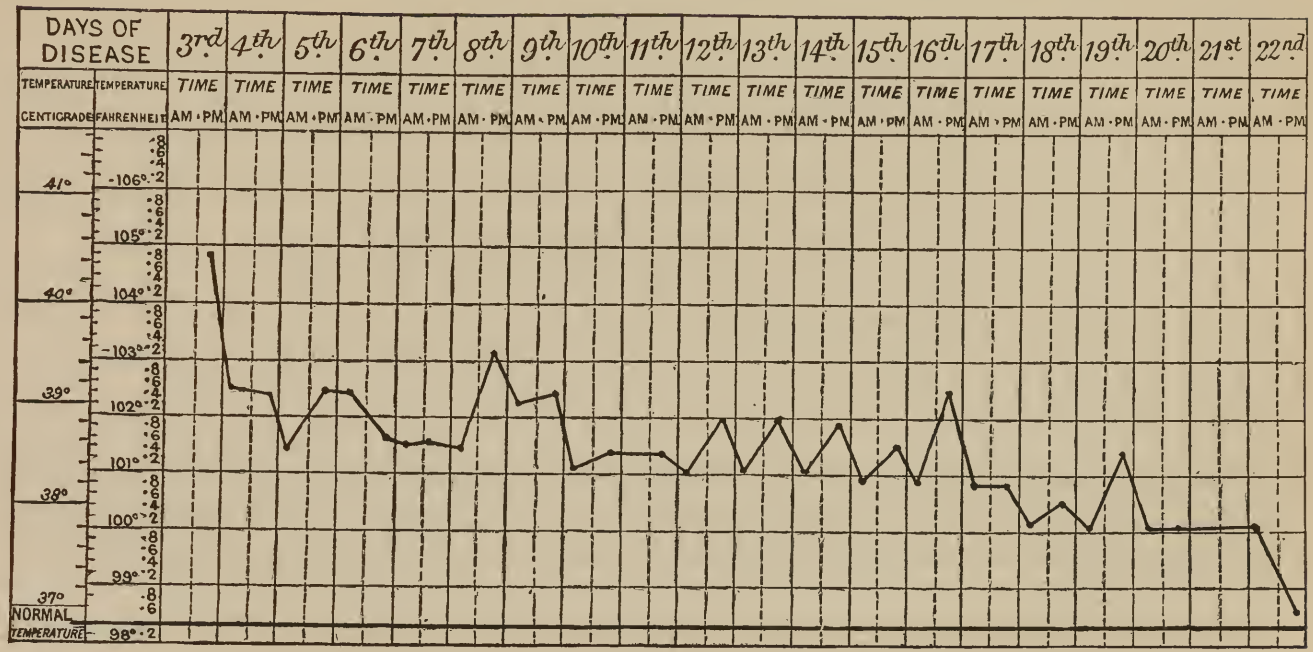
6th. Feels quite well only weak. There is no swelling, and no pain even on pressure over the joints. Acid perspiration continues. Pulse 70; respirations 18; temperature 98°. Heart normal.

He remained well; but took the salicylate three times a day for ten days.

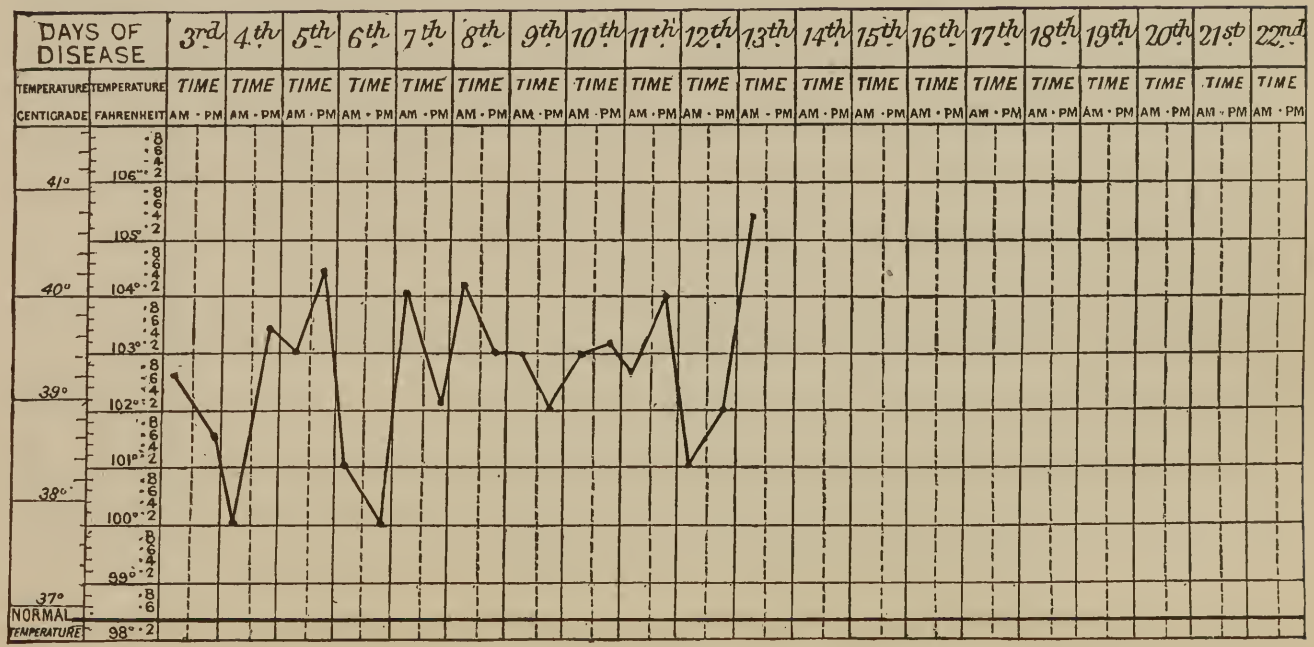
CASE X.—Frederick G——, æt. 22, never had rheumatism before.


CASE VI.
CASE VII.
CASE VIII.
CASE IX.
CASE X.
DAYS OF DISEASE
TEMPERATURE
CENTIGRADE
FAHRENHEIT
NORMAL TEMPERATURE
98°·2
TIME
A.M. P.M

Range of Temperature in a case of acute rheumatism affecting many joints (Wunderlich).



Range of Temperature in a fatal case of acute rheumatism, complicated with Pericarditis. (Sydney Ringer).



December 12, 1877. Present attack commenced four days ago with sore throat and general aching. Now the pain is localized in left knee, both ankles, and right shoulder. Except the shoulder, the affected joints are slightly swollen, and all are distinctly tender, though the pain is not very acute when he is at rest. Any movement aggravates it much. The skin covered with acid perspiration; tongue furred; urine high-colored and loaded with fawn-colored urates; bowels moved by medicine; heart's sounds normal. Pulse 104; respirations 20; temperature 100.8°.

To have twenty grains of salicylate of soda every hour till pain is decidedly relieved; then every two hours.

13*th*. Is much better. Was decidedly relieved after five or six doses of the medicine, but went on with the hourly dose for eight hours. After that he fell asleep, and woke up only now and then during the night. Has had up to this time (11 a.m.) thirteen doses, equal to 260 grains of the salicylate. The joints are stiff and slightly swollen, but the pain is gone. Perspires freely; secretion acid. Pulse 84; respirations 20; temperature 98.8°.

14*th*. Pulse 68; respirations 18; temperature 98.2°. Heart normal. Took the salicylate four times a day for four days, and thrice a day for a week more. Remained well.

These cases suffice to illustrate the controlling power exercised by the salicyl compounds over the rheumatic process.

In young subjects, and in those who have not suffered from repeated rheumatic attacks, such is generally the course of events, if the remedy is given in sufficient quantity, and for a sufficient time. But it is of importance that these two conditions should be observed; for if given in insufficient quantity, the desired result is got slowly, or not at all; and if omitted too soon, the symptoms are apt to recur. On the opposite page is a diagrammatic representation of the range of temperature in these five cases. By way of contrast I have placed alongside of them a similar representation of the temperature range of two cases given in Aitken's "Practice of Medicine"—one of Wunderlich's which recovered, and one of Sydney Ringer's which proved fatal. The difference between these two cases and my own five is too striking for comment. These five are representative of many others.

The tendency to a recurrence of the disease in those treated by the salicyl compounds has been noted by many. In most cases it is attributable to the too early omission of the remedy, or to its administration in insufficient quantity.

The following two cases illustrate this point.

Case XI.—Jane M——, aged 25; had rheumatic fever five years ago. Was then laid up for two months. Present attack began five days ago with *malaise* and pains in limbs.

March 2, 1878. Face flushed and anxious; right knee, ankles, and wrists, swollen and very painful; acid perspiration; tongue furred; urine scanty and loaded with urates; pulse 104; temperature 102.4°. Heart normal. To have light diet, and thirty grains of salicin every hour till pain is relieved; then thirty grains every two hours.

3rd. Took a powder every hour for five hours; after that felt easier, and took one every two hours while awake; has had in all thirteen powders, equal to 390 grains. Is now free from pain; the joints are stiff and slightly swollen, but not tender; pulse 80; temperature 99.8; skin covered with acid perspiration; bowels moved: heart's sounds normal. To have a powder every two hours till a dozen are taken; and then one every four hours for a week, and to remain in bed for that time.

The patient felt so well that she neglected these precautions; got up on the 5th, and took only an occasional powder after that time.

On the 8th the joint pains returned; and on the 9th I saw her with her old symptoms back again, knees, ankles, and wrists inflamed; acid sweats; pulse 100; temperature 101.9°. She had thirty grains of salicin every hour for six hours; and then every two hours.

10th. Is free from pain; pulse 76; temperature 98.5°. Has had 360 grains of salicin. To continue it every three hours for four days, and after that, four times a day for ten days. This time she did as directed, and remained well.

In this case there can be no doubt that the relapse would have been prevented had the patient gone on with the salicin as she was told to do.

What happened was as follows:—

1. The salicin was taken, during the first attack, long enough and in sufficient quantity to destroy nearly, but not quite, the whole of the rheumatic poison.

2. What remained was reproduced, and gave rise to a renewal of the rheumatic symptoms.

3. On the second seizure, the drug was taken for a sufficient length of time, and in sufficient quantity, to destroy the whole of the poison.

4. Convalescence was, therefore, permanent.

CASE XII.—John W——, æt. 44, had rheumatic fever when he was 28 years of age, again when he was 30, a third time when he was 33, and a fourth when he was 37. On the first occasion he was confined to the house for three months, and was unfit for work for other six, nine in all. The second attack was equally long. During the third and fourth attacks he was in bed for six weeks, and off work for three months. Was always treated by potass.

After each attack, chronic shifting pains continued to trouble him for some time after the more acute symptoms had disappeared. When he first returned to work, it took him three quarters of an hour to go a quarter of a mile, so stiff were his joints.

A fortnight ago he began to suffer from twinges of pain in the back, neck, and right leg. Two days ago got much worse, and was obliged to take to bed. For two nights the pains have been so severe that he has had no sleep.

December 1, 1878, 1 *p.m.* Has anxious expression; tongue furred; bowels confined; skin perspiring; perspiration and saliva acid; pulse 116; respirations 30; temperature 102.1°. Has great pain in left heel, all along right leg, and in knee and hip joints of the same side. The neck, and the right wrist and hand, are also painful and tender to touch. The affected parts are tender, but not red or distinctly swollen. The breathing seems a little oppressed. The heart's sounds are free from *bruit*, but are muffled in character; and there is a slight click with the systole. To have an aperient, and thirty grains of salicin every hour.

7 *p.m.* Bowels moved; has had five powders, equal to 150 grains of salicin. Feels altogether better; says he felt easier after second powder; expression improved; can now move his right leg, which he could not do in the morning; moves the arms more freely, and his head with less pain. Has slept more this afternoon than he has done for two nights. Breathing and heart's sounds unchanged; pulse 108; respirations 28; temperature 102.2°. Is perspiring more freely; perspiration acid. Continue powders, one every hour while awake.

2nd, 9 *a.m.* Took a powder every hour till 4 a.m. At that hour he fell asleep, and slept on till eight. Has had up to this time sixteen powders, equal to one ounce of salicin. States that he has no pain, only stiffness of joints and limbs; can bear firm pressure everywhere. Indeed, he felt so well that he got up and at time of visit was sitting in front of the fire, free from pain, but stiff and weak. Skin acting freely; perspiration and saliva acid; pulse 100; respirations 28; temperature 98.4°. States that he can scarcely believe it possible that he is so well. To keep bed, and take thirty grains of salicin every two hours.

8 *p.m.* Has been quite free from pain; so much so that he neglected his medicine, and went from his room into a cold water-closet. Has no pain; but the pulse is 108, the respirations 30, and the temperature 101°. There is a slight click with the first sound of the heart, but the muffled character of the sounds has disappeared.

To remain in bed, and take a powder every hour.

3rd, 10 *a.m.* Had a good night; slept from ten till three without waking; felt quite well then; got up and went to another room to see what o'clock it was; felt weakened and chilled by doing so; slept again from four till seven. Has no pain, but feels weak; perspiration abundant and acid; pulse 92; respirations 28; temperature 98.1°. To have salicin (30 grains) every two hours.

4th. Passed a very good night, awake only once for a short time; feels quite well; heart's sounds normal; acid perspiration continues; pulse 76; respirations 20; temperature 98.2°

At this time I ceased to visit him, but gave strict injunctions that the salicin was to be taken in thirty-grain doses every four hours for a week. Five days afterwards I was sent for to see him again.

Stated that he felt so well that he did not take the medicine regularly, as instructed, but took only half a powder occasionally. Practically the salicin was omitted on the 5th; and on the 7th he put on his clothes and went about the house. The weather at the time was bitterly cold.

On the 8th the pains began to trouble him again.

9th, 5 *p.m.* Has pain in both ankles and right wrist, all of which are swollen and very tender, but not red. Skin hot, not perspiring; pulse 100; temperature 103.3°. Heart's sounds normal. To have thirty grains of salicin every hour

10*th*. After five powders (150 grains) fell asleep, and passed a good night, waking only once. Pain is gone, only stiffness and slight tenderness on pressure remaining; heart normal; pulse 100; temperature 102.7°. Continue salicin every hour. Has had 210 grains in all.

11*th*. Has scarcely any pain, but feels wretched and out of sorts; the joints are not swollen, but are more or less tender on pressure; perspiration acid, not very abundant; pulse 100; temperature 101.5°. Heart normal. Has had 540 grains of salicin. To have thirty grains of salicin and fifteen of bicarbonate of potass every two hours.

12*th*. Is much the same, no special pain; but the tenderness on pressure remains; perspiration slight, but distinctly acid; pulse 100; temperature 101.3°. Continue powders. Has had 750 grains of salicin.

13*th*. Feels much better; pain and tenderness gone; pulse 90; temperature 98°. Has taken 930 grains of salicin.

14*th*. Feels quite well, only weak; pulse 76; temperature 98°. Has good appetite.

He was more careful on this occasion, remained in bed for a week, took salicin for a fortnight, and made a good recovery without any drawback.

In this case the pain was decidedly relieved within six, and was gone within twenty, hours of the time that he came under notice. The temperature, too, had fallen to the normal standard.

It will be noted that during the first attack, neglect of the salicin, on December 2nd, led to a rise of the temperature from 98.4° in the morning to 101° in the evening. Its resumption in hourly doses, led to its speedy fall to the normal.

The second attack was fairly attributable to its early omission.

But the beneficial effects of the salicyl compounds are not always so marked as in the cases which have been given. In those especially who have suffered from repeated and long-continued attacks of acute or subacute rheumatism, these remedies often fail to give the speedy and complete relief which follows their administration in earlier attacks.

The two following cases illustrate this.

Case XIII.—William H——, aged 36; had been subject to rheumatic attacks for sixteen years. The first occurred when he was 20.

Since then has seldom gone more than a year without being laid up with it for some weeks. During the earlier attacks, he was generally laid up for two or three months at a time, but made a recovery which, though slow, was perfect. About six or eight years ago he began to find that the attacks, though really less severe, did not go off as they used to; recovery being less complete, and the joints remaining more or less stiff. As time wore on, and rheumatic attacks repeated themselves, this stiffness became more marked, the pains more constant, and his condition more and more helpless. For two years he has been quite unfit for work; and during the winter and spring unable to go out for fear of catching cold, and making himself worse. Warm dry weather suits him best. The wrists have always suffered much, and are now so stiff that his hands are practically useless. The case, in short, has become one of what is commonly termed chronic rheumatism, varied every now and then by a subacute seizure. These latter occur at irregular periods and intervals. I saw him during one of them in January, 1878. He had been better than usual up to within a week of the time that he came under observation. He had then been confined to bed for four days. His face had an expression of pain and anxiety. Skin moist; perspiration scanty and acid; tongue slightly furred; pulse 96; temperature 100.3°. Urine high-colored, sp. gr. 1.025; no albumen; no sugar; depositing urates on standing. The heart's sounds were normal. The elbows, wrists, fingers, knees, and ankles were stiff, swollen, and painful on pressure and on movement. The wrists, knees, and ankles were most complained of. There was no deformity or alteration in the shape of the joints, except such as was attributable to a general thickening of their fibrous textures. In the wrists this thickening was specially marked.

He was ordered thirty grains of salicin every two hours. On the following day, after 300 grains had been taken, he felt decidedly better, and stated that he had experienced more relief from the powders than from any medicine he ever had before. There was no change in the appearance of the joints, but movement and pressure caused less pain; the pulse was 84, and the temperature 99°. On the next day the pulse was 84, the temperature 98.8°; and he himself feeling better, and comparatively free from pain, so long as he kept quiet. For a day or two more he seemed to improve a little; but it soon became evident that

the salicin was doing no further good—the stiffness and swelling of the joints being undiminished. At the end of seven days, after 1600 grains had been taken, the drug was omitted. During the last three days of its administration its physiological effects were distinct.

Salicylate of soda was then given; twenty grains every two hours for a couple of days; and every three hours for four days more. It produced a feeling of nausea and depression, but did not relieve the pain.

He then got iodide of potass, an opiate at night, and had blisters applied to the affected joints. Under this treatment he improved; the subacute exacerbation was got over; but the state of chronic thickening and pain on movement remained. The patient's circumstances were such that other treatment than that which could be applied at home was inadmissible.

The facts to be noted in this case are, first, the long continuance of the malady; second, the frequency of the attacks; third, the permanent nature of the damage to the fibrous textures; fourth, the good results got from the salicyl treatment during the first day or two of its administration; and fifth, the failure of that treatment to thoroughly remove the symptoms, and rectify the morbid changes.

What had to be dealt with in this case when it came under notice, was an attack of subacute rheumatic inflammation of these altered fibrous textures. There were thus two distinct morbid conditions to be treated: (1) the subacute inflammation of the fibrous textures, due to the direct and present action of the rheumatic poison; and (2) a state of chronic thickening and irritation of these textures, the result of past rheumatic attacks. The salicyl compounds, in virtue of their anti-rheumatic action, allayed the former, but had no action on the latter. Hence their beneficial effects were confined to the first few days of their administration.

The following case exemplifies a less marked, but somewhat similar state of matters.

Case XIV.—George G——, æt. 45; has suffered from rheumatic fever five times, at the ages of 20, 24, 28, 31, and 37. The first three attacks were very prolonged; on each occasion was confined to bed for two months, and unfit for work for four. The last two were shorter,

but his recovery was less perfect, as there seemed to remain some degree of stiffness of the knees, ankles, and wrists.

His present attack (the sixth) began a week ago with pain in the back and limbs. Has been confined to bed for two days. Has had no sleep for two nights, so severe have the pains been.

January 20th. Has pained, anxious expression; tongue furred, and moist; skin covered with acid perspiration; urine scanty, loaded with urates; pulse 112; respirations 26; temperature 102°. Has great pain in right knee and hip, ankles, and wrists; the last-named joints are swollen, and all are tender. Heart's sounds normal. To have an aperient, and thirty grains of salicylate of soda every hour for six hours; after that, every two hours.

21*st.* Has had 450 grains of salicylate (fifteen doses). Says he began to improve after the fourth, and was so free from pain during the night that he slept for three hours on end. The joints are now free from pain except when they are moved or touched; skin covered with acid perspiration; pulse 90; temperature 99.2°. Heart's sounds normal. To have thirty grains of salicylate every three hours.

22*nd.* Slept well; has no pain so long as he remains quiet, but movement brings it back; joints are tender and still slightly swollen, especially the wrists and ankles; pulse 84; temperature 99°; scanty acid perspiration; says the medicine makes him feel sick. To have thirty grains of salicin, instead of the salicylate, every three hours.

23*rd.* Sickness gone; likes the salicin; pulse 80; temperature 98.8°; joints as before.

He went on with the salicin till the 27th. His condition remained unchanged; the joints were slightly swollen, and painful on movement or pressure; the temperature remained from half a degree to a degree above the normal; the secretions continued to be hyper-acid. On the 27th the salicyl treatment was omitted, and he was ordered five grains of iodide and fifteen of bicarbonate of potass in an ounce of water every four hours. Under this treatment he quickly improved; the joints became less tender; the acid state of the secretions gradually passed away; and on the 4th of February he was able to get up. The wrists and ankles remained stiff for some time; they had not quite recovered when he passed from notice. He was last seen on the 19th of February.

The facts to be noted in this case are (1) that the salicyl treatment

speedily allayed the acute symptoms, but failed thoroughly to cure the disease; (2) that after a time it ceased to have any further beneficial influence: and that the potass treatment then did what the salicyl failed to accomplish.

Why was this?

It was, of course, in virtue of its anti-rheumatic action that the salicylate so speedily allayed the acute symptoms. What we have to explain is why it did not thoroughly remove the disease, and make the patient quite well.

The reason is, that in this patient there were two separate morbid conditions to be dealt with. It was his sixth attack of rheumatic fever. The five previous ones had left their mark on him in the form of some thickening and abnormal susceptibility of the textures involved. The two morbid conditions with which we had to deal in the sixth, were: first, the recent inflammation of the fibrous textures, consequent on the present action of the rheumatic poison; and second, the chronic irritation of these textures, produced by the previous rheumatic attacks. The former condition was speedily allayed by the salicyl treatment; the latter was one over which such treatment could have no control.

The lactic acid formed during the early days of the sixth seizure no doubt kept up this irritable state of the fibrous textures; and it was probably by counteracting this agency, and aiding in its elimination, that the alkaline treatment did so much good; it relieved the altered fibrous textures from the irritating action of that acid, and permitted them to return to the condition in which they were prior to the sixth seizure.

These two cases serve to illustrate a morbid condition which it is of much importance that we should recognize. It is a sequence of rheumatism, rather than a distinct form of the disease. It essentially consists in chronic thickening and irritability of fibrous textures which have been the seat of repeated rheumatic attacks.

The history of acute rheumatism abundantly shows, what a very slight knowledge of pathology would indicate, that the textures which have been the seat of inflammation, do not recover their natural tone as soon as the inflammation ceases. There always remains for a time, which varies with the length and severity of the seizure, some thickening of the fibrous textures of the affected joints, causing the stiffness

which is felt after the acute symptoms have disappeared. If the attacks are frequent and obstinate, this morbid change in the fibrous textures is less and less perfectly recovered from: by each succeeding seizure a little more damage is done; and ultimately there is induced a condition of chronic thickening of these textures, which is permanent.

That such a change should take place as a result of frequent and long-continued rheumatic attacks, consists with what we know of the mode of production of similar pathological changes in other organs. Sir William Jenner has shown—and all pathologists admit the accuracy of the observation—that the continued presence in an organ of an increased quantity of blood, gives rise to induration of its substance—that is, to increase of its fibrous tissue. If such a change occurs in organs like the liver and kidney, of whose structure fibrous tissue forms a comparatively small part, it is much more likely to occur in ligaments and capsules which are composed entirely of it.

Clinical experience likewise teaches that, when an organ has been the seat of repeated attacks of inflammation, the local symptoms to which such inflammation gives rise, are apt to recur in a minor degree from the operation of causes which would not have sufficed to induce the original attack. What more common than for chronic bronchitis to be developed as a sequence of one or more acute attacks; and for the course of the chronic malady to be interrupted by subacute seizures, brought on by causes which would not have sufficed to induce the original malady?

A similar instance we have in the readiness with which dysenteric symptoms may be developed in those who have once suffered from the acute form of the disease. Exposure to cold, overfatigue, mental disturbance—causes which could never have originated the disease—will often bring back some of the local symptoms of the original attack in a milder, but still quite characteristic, form.

So it is with fibrous textures which have been weakened and altered by repeated rheumatic attacks. They are rendered irritable and weak by the changes which have taken place in them, and are apt to be disturbed by agencies which have no effect on healthy fibrous textures. Irritation of fibrous textures, no matter how induced, causes pain in the affected part. Hence such disturbance as arises in these altered textures from exposure to cold and damp, gives rise to the same symp-

toms as would result from the action of the rheumatic poison. Originating in true rheumatic attacks, occurring in those who have given decided evidence of being of rheumatic constitution, and characterized by symptoms which are associated with true rheumatism, it is not unnatural that the symptoms should be regarded as due to the action of the rheumatic poison. But such a view is pathologically inaccurate, and pregnant with therapeutic errors. The condition which has to be dealt with is one which, though originally induced by repeated rheumatic attacks, exists, after it has been developed, independently of the cause which gave rise to it. It bears a resemblance to that which frequently follows mechanical injury to the fibrous textures of a joint. When a joint is severely strained, there is more or less injury to the capsule, ligaments, and tendons. This may be so great as to cause permanent change in, and thickening of, these textures. Such altered tissues are frequently the seat of pain which is indistinguishable from that of rheumatism; and such pain is frequently induced by cold, damp, or other disturbing cause.

It is the same with the altered state of the fibrous textures, which results from repeated rheumatic attacks; cold, damp, east wind, change of weather, suffice to induce the same troublesome pain which was originally caused only by the rheumatic poison.

This morbid condition exists in various degrees. The early stage of its development is instanced in Case XIV.: a more fully developed stage in Case XIII.

These are the cases in which the salicyl treatment fails to effect a cure.

When the fibrous textures are in this altered and susceptible state, irritation may be set up in them by other causes than the rheumatic poison. No matter how induced, the symptoms of such irritation are always the same. Pain, swelling, slight rise of temperature, even increased formation of lactic acid, may thus result from inflammation of these altered fibrous textures induced by cold, just as like symptoms would result from similar disturbance set agoing by the rheumatic poison. We may thus have all the symptoms of subacute rheumatism, without any action of the rheumatic poison. Over such an attack, the salicyl compounds can exercise no control.

If the subacute exacerbation be due to the action of the rheumatic

poison, the salicyl treatment will do good for a time, but will fail to cure, because the irritable textures will take some time to regain their normal condition, after the rheumatic poison has ceased to act; and because the lactic acid, formed as a result of their inflammation, tends to keep up disturbance in them. Such a case treated by salicin or salicylic acid would be, and with justice, instanced as one in which these compounds gave only partial and temporary relief.

If the subacute exacerbation were due to the action of cold or exposure, the salicyl compounds would have no remedial effect; and the case would, with justice, be given as an instance in which these compounds failed to give any relief, though given in full and frequent dose.

It is in these cases in which the fibrous textures have been the seat of prior attacks of rheumatic inflammation, that the alkaline treatment often does much good. The change resulting from the former attacks, renders these textures more irritable, and more liable to disturbance from the presence of lactic acid. As a consequence of this, the local symptoms are apt to persist for a time after the action of the rheumatic poison has ceased. They are kept up by the lactic acid; and anything which hastens the elimination of this from the system, tends to shorten the duration of the attack. Hence in such cases the alkaline treatment should be combined with the salicyl. The latter puts a stop to the rheumatic process; the former aids in the elimination from the system of the lactic acid formed during it.

When it is a first or second attack with which we have to deal, the salicyl treatment suffices to effect a rapid cure. But when the patient has suffered from repeated attacks, and when, as a consequence of these, more or less change has been induced in the fibrous textures of the joints, there can be no doubt that alkalies tend to shorten the duration of the malady. They do so by neutralizing the lactic acid, and aiding its elimination by other organs than the skin. They do not cure the rheumatism properly so called; but they hasten the elimination of morbid products formed during its course.

As compared with the frequency of the occurrence of the acute and subacute forms of rheumatism in which it originates, this chronic thickening of the fibrous textures is not common, at least in its fully developed form. For this there are two reasons: first, it is only in a minority of cases that the rheumatic constitution is so marked as to lead

to attacks sufficiently frequent and long-continued for its production; and second, in a large number of those who possess this markedly rheumatic constitution, the heart suffers as well as the joints, and death ensues from the cardiac trouble before there has been time for the development of permanent thickening of the fibrous textures.

Nowadays, treatment is so successful in shortening the duration of acute and subacute rheumatism, that it may reasonably be hoped that this condition will year by year become less common. Meantime, there are many such cases. The existence of these makes it necessary that the true nature of the ailment should be recognized.

Chronic thickening of the fibrous textures is a condition over which drugs exercise little or no control.

One never can be quite sure that the pain at a given time may not be due to the present action of the rheumatic poison. The salicyl compounds should, therefore, always be given for a time, not with the idea of removing the chronic thickening, but with the object of relieving any purely rheumatic symptoms.

Iodide of potass, arsenic, guaiacum, sulphur baths, and other remedies, may be tried. For those who can afford it, the treatment of some of the baths of France and Germany, holds out the best prospect of relief. For those who cannot go there, that treatment should be, as nearly as may be, imitated at home. Blisters and rubefacients often afford considerable relief.

Chronic rheumatism is the ailment for which this condition of chronic thickening of the fibrous textures is most apt to be mistaken. Occurring, as the latter does, in those who have suffered from repeated attacks of acute or subacute rheumatism, and presenting, as it does, many of the symptoms of rheumatism, it could scarcely fail to be mistaken for the chronic form. It is of great importance that the two ailments should not be confounded, for their prognosis and treatment are essentially different.

Wherein chronic thickening of the fibrous textures consists, its name implies. Its pathology we have just considered.

Chronic rheumatism, properly so called, is a very different condition. It is due to the presence and direct action of the rheumatic poison, and is not necessarily, or even usually, accompanied by any perceptible change in the textures involved. It consists simply in rheu-

matic disturbance of the affected tissue. It differs from the acute and subacute forms—not in nature, but in degree, and sometimes in the special textures involved. It is a true rheumatic attack, in which the morbid process and local disturbance are not sufficiently marked to raise the temperature, or to lay the patient up.

The textures involved are the same as those which suffer in the acute and subacute forms, with this difference, that the fibrous aponeuroses and muscles are more apt to be affected.

Indeed, for clinical purposes, cases of chronic rheumatism might usefully be divided into two classes—chronic articular rheumatism, and chronic aponeurotic or muscular rheumatism.

Chronic articular rheumatism usually affects the same joints as suffer in the acute and subacute forms.

Seldom more than one or two joints are affected at the same time; and in none of them is the pain bad enough to lay the patient up. It shifts from joint to joint, and may last, off and on, for months or even for years, the patient during the whole time being never really ill, and yet never quite well for more than a few weeks at a time.

The following two cases serve to illustrate this form of the disease.

Case XV.—Mrs. S——, æt. 34, the mother of seven children; had rheumatic fever when she was 15. Was in bed for three months at that time. At 27 had a second, but much milder attack, which lasted only for eight or ten days. States that she had been subject to joint pains almost ever since her first attack. Is frequently quite well, and free from pain; but for last six months has had it very constantly, but never bad enough to prevent her going about.

May 12, 1877. Has been ailing all the winter. For last six weeks has not been out of the house, as going out always made her worse. Has now pain and stiffness of knees, ankles, and wrists; the last are a little fuller than natural. Heart normal; pulse 70; temperature 98.5°. To have thirty grains of salicin every three hours.

14*th*. Feels better than she has done for months. Pain nearly gone. Has taken thirteen powders, equal to 390 grains of salicin.

16*th* With the exception of a little stiffness of the joints, feels quite well. Is free from pain.

A year and a half afterwards she consulted me about one of her children. Told me that the salicin did her so much good that she had taken it, off and on, almost ever since. Has never enjoyed such good health, or been so free from pain as during the last year.

Case XVI.—James K——, æt. 35. Had an attack of rheumatic fever when 18 years of age. Was laid up for two months. Has suffered from occasional pains in the joints almost ever since. Thinks he has never been more than three months on end quite free from pain. Its usual seats are the knees, ankles, and wrists. Generally only one joint is affected at a time. For the last few months the pain has been more troublesome, especially in right knee.

December 8, 1878. Has pain and stiffness of right knee and ankle. Neither joint is swollen, but each is tender on firm pressure. Heart's sounds normal; pulse 74; temperature 98.6°. To have thirty grains of salicin every two hours.

9*th*. Feels decidedly better.

11*th*. Is free from pain, and more comfortable than he has been for many months. Has had in all 360 grains of salicin.

He continued it three times a day, in twenty-grain doses, for several weeks; and by my advice took it for some months twice a day.

In December, 1879, he wrote to me as follows:—"It is just a year since you prescribed the salicin for me. I thought it might interest you to know that I have continued to take it ever since, off and on. The dose I take is twenty grains once or twice a day. I have never passed more than a week without it. I was never better in my life than I have been during the past year, and never so free from pain."

The heart is less apt to suffer in the chronic than in the acute and subacute forms; but it does sometimes become involved, as in the following case.

Case XVII.—John M——, æt. 38, a medical man, consulted me in November, 1878, regarding some cardiac symptoms from which he was suffering. The heart was much enlarged, there was marked regurgitation at both aortic and mitral orifices.

He stated that he began to suffer from occasional rheumatic pains

in 1867, and that he has done so more or less ever since. Was never so bad as to keep the house, except for about a fortnight in 1869. Pain has generally been in knees or ankles, occasionally in the elbows, but seldom in more than one joint at a time. The left knee was the chief seat, but it shifted about very frequently. Has never felt unfit for work except on the occasion referred to, in 1869. Has been short of breath for some time, but always regarded it as asthmatic in nature. The left knee is now occasionally the seat of pain.

The cardiac ailment increased; and he died of it two months after I first saw him.

Rheumatism of the muscles and aponeuroses, is nearly always chronic. Occasionally in the course of an acute or subacute attack, the aponeuroses, especially that of the thigh, may be affected. But such rheumatism, occurring by itself, independently of the articular form, is rarely other than chronic.

It is more common in women than in men. When it occurs in man, it is generally at a more advanced age than the acute articular form.

Its chief seats are the loins, thighs, and shoulders.

Whether or not the fibrous aponeuroses ever suffer without the muscles being involved, and whether or not the muscles ever suffer without the aponeuroses being affected, are points which it is impossible accurately to determine—so intimately are the two structures blended together.

The chief symptom of this form of rheumatism is pain, dull and aching in character, increased by movement and by pressure, varying in degree, but not so apt to shift about as that of the articular form of the malady.

The ailments for which it is most apt to be mistaken, are chronic gouty pain, and neuralgia.

From the former it is to be distinguished by the age, sex, and history of the case. The gouty state is most common in men; and there is generally evidence of its existence, either in prior attacks, or in the present state of the joints, or general health.

From neuralgia it is distinguished chiefly by the situation, and dull aching character, of the pain. Neuralgia of the loins and thighs is generally due to uterine disease.

The following cases illustrate this form of rheumatism.

CASE XVIII.—Mrs. F——, æt. 25; had for several months suffered, off and on, from pains in shoulders, loins, and right thigh. During the last few weeks they had got worse. Pain is increased by motion. Never had rheumatic fever, or any affection of the joints. She has no other local ailment, but feels weak and out of health. This she attributes to pain and want of sleep. Pulse and temperature normal. To have twenty grains of salicin every two hours till the pain is relieved; and then three times a day for a fortnight.

Three weeks later she again consulted me. Stated that the powders quite cured her in three days, and that she then omitted them. A week after she omitted the salicin, the pains returned in the old localities. It was again given in twenty-grain doses every two hours for three days; after which time she was ordered to take a powder three times a day for three weeks. This she did; and with the result that the pain disappeared, her general health improved, and she remained well.

CASE XIX.—Mrs. P——, æt. 28; never had articular rheumatism; had suffered for six weeks from pain in both thighs, hips, and lumbar region. Affected parts are somewhat tender to pressure made with the point of the finger, but not to similar pressure with palm of hand. The tenderness is most marked over upper and outer parts of thighs. Has been rubbing on various anodyne and stimulant applications, without relief. Pulse and temperature normal. To have twenty grains of salicin every two hours.

On the following day she was decidedly relieved; and on the next, after having taken in all 360 grains, was all but free from pain.

She took twenty grains of salicin three times a day for a fortnight, and remained well.

As will be seen from these cases, the treatment of this form of rheumatism is not different from that of the articular form of the disease.

The cases which have been given, serve to illustrate the controlling power exercised by the salicyl compounds over the rheumatic process.

It remains for us to consider how this power is exercised—how the salicyl compounds produce their anti-rheumatic effect.

CHAPTER XVI.

THE MODE OF ACTION OF THE SALICYL COMPOUNDS IN RHEUMATISM.

Between rheumatic and intermittent fevers there exist not only pathological but therapeutic analogies. The pathological analogies have already been dealt with. The therapeutic have now to engage our attention.

It is scarcely possible to study the therapeutic effects of the salicyl compounds in acute rheumatism, without comparing them with those of quinine in ague. The analogy forces itself on our notice.

Either remedy manifests its effects by a prompt alleviation of all the symptoms of the disease; to ensure its full beneficial action, each has to be given in large and frequently repeated dose, and for some time after the acute symptoms have disappeared; and neither produces the same marked effects in any other ailment.

Holding, as we do, that the poisons of rheumatism and of ague, though specifically distinct, are similar in nature and in mode of action; and finding that the morbid process to which each gives rise may be arrested by large doses of somewhat similar remedies, we cannot but regard it as at least probable that the mode of action of the remedy is the same in both—that the salicyl compounds cure rheumatic fever in the same way that the cinchona compounds cure intermittent.

How each exercises its curative effect is the question which we have now to consider.

Let us first take the cinchona compounds.

That the cinchona alkaloids arrest the course of intermittent fever is an established fact in practical therapeutics. How they do so has never been explained. "Ague is the disease of all others in which the power of medicine, both as regards prophylaxis and treatment, is most marked. We know that if a man pass through certain districts, and more especially if he sleep in them, he is likely to be attacked with a fit of shivering which, after lasting some time, will be succeeded by a

burning fever, and then by profuse sweating, after which he will feel comparatively well until the next day, when another shivering fit will come on at the same hour and run the same course as the first. We know that by warning the man against the dangerous locality, or by making him adopt certain precautions, take cinchona alkaloids, if he cannot avoid the place, we may be able to prevent the disease; by administering one large dose of quinine before a paroxysm we may stop its approach, and by continuing the remedy we may prevent its recurrence altogether. But we have no notion of the manner in which quinine counteracts the malarial effects."

There are two ways in which the curative effects of quinine in ague may be produced: either the quinine may so act on the system as to render it insusceptible to the action of the ague poison; or it may so act on that poison as to deprive it of its power of affecting the system. In other words, the action of quinine is either on the system, or on the poison. Let us inquire which it is. And first, let us take its action on the system.

Quinine in large dose (10 to 30 grains) possesses in a remarkable manner the power of lowering the temperature of the body, when unduly elevated. How it exercises this power is not known.

It has been supposed to be due to a special action of the quinine on the nervous centres; and if we recognize the existence of a special thermic centre, regulating the production and distribution of heat, as the vaso-moto centre regulates the distribution of the blood—a supposition in favor of which much may be said—this explanation might be regarded as a very feasible one.

Binz thinks this effect of quinine is to be explained by its lessening the ozonizing power of the blood, and so checking oxidation. All that we really know, and all that concerns us at present, is that quinine in large dose lowers febrile temperature. What we have to consider is whether or not its curative effect in intermittent fever is due to this property, or to some other and special remedial action.

In virtue of its febrifuge properties, quinine has been administered in all febrile ailments. It was at one time claimed for it that it pos-

[1] Pharmacology and Therapeutics, by T. Lauder Brunton, M.D., F.R.S. 1880.

sessed the power of cutting short typhus. More recently it has been claimed for it, as for other febrifuge remedies (the cold bath and salicylic acid), that it exercises a distinctly curative action in typhoid fever, and shortens the duration of that malady. But this conclusion is not supported by the evidence. There is no proof that quinine either shortens the duration, or lessens the dangers, of either typhus or typhoid fever; or that it exercises a distinctly curative and curtailing effect in any other form of fever than intermittent and remittent.

The point is one which could be readily proved, and would long ago have been proved had the facts been as some have stated them to be.

I have frequently given quinine in large dose in all febrile ailments. My experience entirely coincides with that of Murchison, who says, with reference to both typhus and typhoid fevers, that he had "seen no evidence that, at whatever stage it was given, it shortened the course of the disease or diminished its danger."[1]

With the exception of the external application of cold, quinine, given in large dose, is the most powerful febrifuge remedy we possess. There is probably no febrile ailment in which it might not pull the temperature down. But in every such ailment, except intermittent and remittent fevers, this depression is temporary. While the temperature is lowered by quinine, the morbid process which constitutes the disease still goes on; by-and-by the antipyretic effect of the drug passes off, and the disease runs its course, uninfluenced by what has taken place.

So it is with all the continued and communicable fevers. Quinine has no power to arrest their course. Where there is trouble or danger from mere elevation of temperature, it may do good by lowering this. But there its usefulness ceases.

In intermittent fever the case is very different. Here the quinine actually cures. It puts a stop to the whole morbid process, and all that constitutes the disease; and it does this so constantly, so speedily, and so certainly, and its beneficial effects are so lasting, that one cannot fail to see that they are altogether peculiar, and altogether different from those got from its administration in other febrile ailments.

That the action of quinine in arresting the course of intermittent fever is not to be explained solely by its febrifuge properties, is further

[1] Murchison, op. cit.

shown by its power of preventing such fever. Given during the intermission, it prevents the fever from coming on. It exercises a distinctly prophylactic action. Taken regularly by those living in malarial districts, it prevents them from suffering from the action of the poison of intermittent fever. It exercises no such action in any other febrile ailment.

Besides its febrifuge property, quinine possesses no other special action on the body by which its curative effect in ague can be explained. This property does not account for its remarkable power of arresting the progress, and guarding against the occurrence, of that disease. We are thus forced to the conclusion that the curative effect of quinine in intermittent fever, is not to be explained by any action which that drug exercises on the system.

The only alternative view is that it acts on the poison of intermittent fever, and deprives it of its power of affecting the system.

There are two ways in which quinine might deprive the ague poison of its morbific action. It might supply to the poison the second factor requisite to its propagation, and so prevent it taking this from the system; or it might simply destroy the poison.

The first is extremely unlikely. Indeed it is difficult to find anything to say in support of it, except that it is possible. It is not at all certain that such an action might not be accompanied by considerable disturbance. But even if it were not, it could scarcely result in a cure of the disease. It would simply lead to the continued development of the ague poison during the whole period of the administration of the quinine, and to an outbreak of the disease when the drug was stopped. For the large quantity of poison which, on this view, would necessarily exist in the system at that time, would find there the material necessary to its growth and propagation, and consequent morbific action, just as it would have done had quinine never been given.

The view that quinine acts by destroying the malarial poison, has much more to commend it.

Regarding this poison, as we do, as a minute organism, there is nothing improbable in the view that quinine should exercise a destructive action on it; for we know, from the investigations of Binz, that quinine possesses in a remarkable manner the power of destroying many minute organisms.

It thus consists, both with what we believe regarding the ague poison, and with what we know regarding the action of quinine, that the latter should have the power of destroying the former.

It is scarcely necessary to point out that the possession of this power would quite explain both the prophylactic and curative actions of quinine in intermittent and remittent fever.

That such is really the mode in which quinine acts in these maladies, seems to me in the highest degree probable.

We were led to consider this mode of action by the failure of the only alternative mode, viz., its action on the system, to explain the curative effects of the drug. We are led to adopt it by finding, not only that it explains that action, but that this explanation consists with all that we believe regarding the nature of the ague poison, and all that we know regarding the action of quinine on minute organisms, such as we believe the ague poison to be.

But, it may be said, if quinine owes its curative effects in intermittent and remittent fevers to its power of destroying minute organisms, why is it only in these maladies that this curative power is manifested? There are many other ailments which are believed to be produced in the same way, but in not one of them does quinine have the same power of arresting the morbid process.

In the natural history of minute organisms there is no fact better established than that such organisms are possessed of specific differences of whose existence their external form gives no evidence. Two organisms may be indistinguishable from each other by the highest powers of the microscope—so far as can be made out by such examination, they are identical. But it may be found that the one flourishes under conditions which are fatal to the other. In the case of parasitic organisms, this is specially observed; each has its own habitat, in which alone it flourishes, and in which other organisms die.

Again, an agency which destroys one organism may have no effect on another; though the two may be apparently identical. A remedy, therefore, which cures one disease by destroying the organism which gives rise to it, does not necessarily cure all diseases owning a similar causation. Hence quinine may cure intermittent and remittent fevers by destroying the organism which produces them, without having a

like destructive effect on the organisms which give rise to diphtheria, small-pox, scarlatina, typhoid fever, etc.

Poisons possessed of specific differences may have these differences manifested, not only by the different effects which they produce on the system, but by the different effects which other agencies have on them.

The fact that quinine does not shorten the duration of all diseases caused by the propagation of minute organisms in the system, is no proof that it does not owe its power to cut short intermittent fever, to a destructive action on the organism which gives rise to that malady. The fact that it does cut short this fever, is to be accepted as a hopeful indication that other remedies may be found capable of exercising a similarly beneficial effect on other forms of fever whose course we are now powerless to control.

It is, indeed, in the recognition of this view—that the curative effect of a drug may be due to its action on the poison of the disease, rather than on the system in which it occurs—that lies the main hope for the future discovery of remedial agencies, calculated to arrest the course of maladies which owe their causation to the propagation of minute organisms in the system. The discovery of the anti-rheumatic action of salicin was the result of no hap-hazard experiment; but a legitimate inference drawn from the views which I held, first, regarding the nature and mode of production of rheumatism; and second, regarding the mode of action of quinine in those diseases to which rheumatism is most nearly allied.

It was the belief (1) that the rheumatic poison was allied in nature to that of intermittent fever; (2) that both were minute organisms; (3) that the morbific effects of each were due to its propagation in the system; (4) that the curative effects of the cinchona compounds in intermittent fever, were attributable to their destructive action on the poison of that disease;—it was this belief that led me to the conclusion that salicin was not unlikely to exercise a like destructive action on the poison of rheumatism. If quinine destroyed the poison of intermittent fever, it seemed to me, for reasons already given, that salicin was not unlikely to exercise a like destructive action on that of rheumatism, and a like curative effect on the disease to which it gave rise. That it does produce this curative effect has been abundantly demonstrated. The

success of the practice is an argument in favor of the pathological and therapeutic views on which it was founded.

All that has been said regarding the action of the cinchona compounds in ague is, *mutatis mutandis,* applicable to the action of the salicyl compounds in rheumatism.

The analogies which are believed to exist between the poisons of intermittent and of rheumatic fever, have already been pointed out. We regard each as a miasmatic organism which is reproduced in the system, which owes its action to such reproduction, and which is destroyed during the course of the disturbance to which it gives rise.

Between the cinchona compounds and the salicyl compounds there are also marked analogies.

1. The most prominent of these, is the power which each possesses of curing a miasmatic fever. The cinchona compounds cure intermittent, the salicyl compounds cure rheumatic fever.

2. The cinchona compounds are possessed of no physiological action by which their power to arrest the course of intermittent fever can be explained.

It is the same with the salicyl compounds. On the non-febrile body they have no action by which their curative effects in rheumatic fever can be accounted for.

3. It was at one time hoped, and has been at various times asserted, that quinine would arrest the course of other fevers than intermittent and remittent. But though it has been established that quinine in large dose lowers the febrile temperature, often several degrees, it has been equally established that this effect is only temporary, and that the only fevers in which it exercises a distinctly curative action, are intermittent and remittent.

It is the same with the salicyl compounds. It has been hoped, and over and over again asserted, that they possess a curative action in the same febrile ailments over whose course quinine was at one time believed to exercise a controlling influence. But the result has been the same as with the cinchona compounds. Though the salicyl compounds have been proved to be possessed of febrifuge properties, they exercise no distinctly curative effect in any febrile ailment except acute rheumatism.

As febrifuges they are much inferior to quinine. I have frequently

seen a couple of ten-grain doses of quinine, given the one an hour after the other, lower the temperature three or four degrees, after several hourly thirty-grain doses of salicylate of soda had failed to have any effect.

But though the salicyl compounds possess the febrifuge property to a less extent than the cinchona compounds, they are not devoid of it. Salicylic acid especially possesses this property very distinctly. And we have now to inquire whether or not their beneficial action in acute rheumatism is due to this, or to some other special curative effect.

It is with the salicyl compounds in rheumatism as with the cinchona compounds in ague—there are but two ways in which their remedial action can be explained. Either they so act on the system as to render it insusceptible to the action of the rheumatic poison; or they so act on the rheumatic poison as to render it incapable of acting on the system. One of these it must be; for there is no other possible.

First, as to their action on the system.

Like quinine, the salicyl compounds have no effect on the temperature of the non-febrile body; but possess, in an undoubted manner, the power of lowering that of the febrile body. Salicylic acid possesses this property to a much greater extent than salicin.

To produce its antipyretic effect, salicylic acid requires to be given in much larger dose than quinine; and even then its action is less certain and less decided than that of the cinchona alkaloid.

In virtue of its febrifuge properties, it has been administered in nearly all febrile ailments, with varying results. Riess has maintained that it shortens the duration of typhoid fever. I have given it freely in both typhus and typhoid fevers, and never found any evidence that it either shortened the duration, or diminished the mortality, of either of these maladies. This seems to be the experience of most observers.

Were Riess right on this point, the accuracy of his statement would have been placed beyond doubt before now; for salicylic acid was freely used in typhoid fever before it was given in acute rheumatism. Its remedial power in the latter was matter of demonstration five years ago, and is every year made more certain. Its remedial power in the former has never been demonstrated; and evidence is every day accumulating to show that Riess erred in attributing such an action to it. On

several occasions it has seemed to me to exercise a depressing and injurious action.

Evidence all tends to show that it is with the salicyl compounds, as with the cinchona compounds—they are possessed of undoubted febrifuge properties, but there is but one febrile ailment in which they are known to exercise a distinctly curative effect. In other fevers they may for a time lower the temperature, but they do not materially alter the course, or curtail the duration, of the malady. In rheumatic fever alone they put a stop to all that constitutes the ailment—the local inflammation and pain, as well as the general febrile disturbance.

Acute rheumatism does not consist solely of fever. An essential part of its existence is inflammation of the fibrous textures of the motor apparatus.

Just as it is impossible for any poison to produce the disease without causing inflammation of these textures—so it is impossible for any remedy to cure it, without allaying that inflammation.

The fever and the local inflammation are essential parts of the disease. Fever does not cause inflammation, but inflammation does cause fever. A remedy which acted solely as a febrifuge, could not allay the inflammation. But a remedy which put a stop to the inflammation, might allay the fever.

The febrifuge property of the salicyl compounds is inadequate to explain their power to arrest the course of acute rheumatism. In virtue of that property they might allay the fever, but could not, without some other action, arrest the local inflammation.

But besides their febrifuge effect, the salicyl compounds have on the system no other action by which their power to arrest the course of acute rheumatism can be explained.

In health they have absolutely no action on the fibro-serous tissues of the motor apparatus.

When these tissues are inflamed from other than rheumatic causes, they are equally without action, and have no power to allay that inflammation.

But when they are the seat of rheumatic inflammation, no matter how acute, the salicyl compounds exercise over that morbid process a remarkable controlling influence.

Were it simply in virtue of their febrifuge properties that the salicyl

compounds cured acute rheumatism, their beneficial action would not be confined to that disease, but would be equally manifested in other febrile ailments: and that, we know, is not the case.

Again, the salicyl compounds have less febrifuge power than quinine and the cold bath. Were a febrifuge action that by which the cure of acute rheumatism is effected, quinine and the cold bath would be more serviceable than the salicyl compounds; but they have little or no anti-rheumatic action.

We are thus driven to the conclusion that the anti-rheumatic effects of the salicyl compounds are not to be explained by any action which they have on the system—febrile or non-febrile.

There remains only their action on the rheumatic poison.

As already remarked, there are two ways in which the salicyl compounds might so act as to deprive the rheumatic poison of its power to affect the system. They might supply to that poison the second factor requisite to its propagation; and so prevent it taking this from, and acting on, the fibrous tissues. Or they might destroy the rheumatic poison.

The former supposition is a very improbable one. It is difficult to find anything to say in support of it, except that it is possible. Against it, there is the same argument which applied to the case of quinine under similar circumstances. It would lead to the propagation of the rheumatic poison in the system during the whole period of administration of the drug, and to a sudden outbreak of rheumatic fever when its administration ceased.

The view that the salicyl compounds owe their anti-rheumatic effects to a destructive action on the rheumatic poison, has much more to commend it.

If that poison be a minute organism, there are good *a priori* grounds for regarding this explanation as at least a probable one; for the salicyl compounds are known to possess in a remarkable manner the power of destroying minute organisms. Salicylic acid was first introduced to notice as an antiseptic, *i.e.*, as an agent possessing the power to arrest those processes which are associated with, if not actually dependent on, the growth of minute organisms. For this reason, it has been administered in all diseases whose poisons were believed to be organized—diphtheria, scarlatina, typhoid fever, etc. Its administration in acute

rheumatism by the German physicians, was a pure piece of empiricism; and the results obtained matter of surprise rather than of expectation.

The views advanced in these pages as to the nature of the rheumatic poison, and as to the mode of action of the salicyl compounds, afford a scientific basis for this practice, and an adequate explanation of its success.

It has already been explained that I used salicin in the treatment of acute rheumatism more than a year before salicylic acid was brought into notice by Stricker and Riess; and that my employment of it was not a piece of empiricism, but a logical inference deduced from the views which I then held, and now advocate—first, regarding the nature of the rheumatic poison; and second, regarding the mode of action of quinine in intermittent and remittent fevers.

It need scarcely be pointed out that this view of the mode of action of the salicyl compounds, adequately explains their curative effects in acute rheumatism. It is the view, too, to which we have been driven by the failure of every other possible one to stand the tests of examination and inquiry. It alone stands these tests, and fulfils every requirement of a satisfactory theory. We accept it, not only because it does so, but because there is no alternative between it and blank ignorance.

The objection may be raised, that if the salicyl compounds possess the power to destroy minute organisms, their curative effects should be manifested in other ailments produced in the same way, and not be limited to acute rheumatism.

The answer is that already given to the same objection applied to the case of quinine:—poisons possessed of specific differences, may have these manifested, not only by their different effects on the system, but by the different effects which other agencies have on them

The fact that the salicyl compounds do not shorten the duration of other febrile maladies, is no proof that they do not owe their power to cut short acute rheumatism to their destructive action on the rheumatic poison.

The salicyl compounds form a numerous and remarkable series. There are in all some thirty or forty substances included in it. The chief of these are:—

	Formula.
Salicin	$C_{13}H_{18}O_7$
Saligenin	$C_7H_8O_2$
Saliretin	C_7H_6O
Salicylous acid (oleum spiræae)	$C_7H_6O_2$
Salicylic acid	$C_7H_6O_3$
Methyl salicylate (oil of winter green)	$CH_3C_7H_5O_3$
Helicin	$4C_{13}H_{16}O_7 3H_2O$
Salicyluric acid	$HC_9H_8NO_4$

Though this table represents not a fourth part of the salicyl compounds, it serves to show the composition of those with which we shall have to deal. It will be seen that, with the single exception of salicyluric acid, which contains a little nitrogen, they are all composed of carbon, hydrogen, and oxygen.

The basis of the whole series is the radicle salicyl ($C_7H_5O_2$), a substance which has never been isolated.

Of all the salicyl compounds, the only two which have hitherto been used in medicine are salicin and salicylic acid.

Salicin is extracted from the bark of various species of willow. It is a white crystalline substance, having a bitter taste. It is sparingly soluble in water.

When boiled for a few minutes with dilute sulphuric or hydrochloric acid, it is converted into glucose and saligenin, which latter may, after agitation with ether, be separated in a crystalline form. The same change takes place when salicin is allowed to remain in a solution of synaptase—the salicin is split up into saligenin and glucose. The solution strikes a deep blue color with ferric chloride. Salicin itself gives no such color.

If the boiling with the acid be continued for some time, the saligenin itself is destroyed, and there is formed a resinous substance called saliretin.

When salicin is acted on by a powerful oxidizing agent, such as chromic acid, the change does not stop at the formation of saligenin and sugar. These substances are also decomposed: the sugar producing formic acid, and the saligenin yielding a fragrant oily liquid, which is salicylous acid, or oleum spiræae.

Saligenin and saliretin also yield this oil, when treated with chromic acid. The change which takes place is simply one of oxidation; thus:—

$$\overbrace{2C_7H_8O_2}^{\text{Saligenin.}}+O_2=\overbrace{2(HC_7H_5O_2)}^{\text{Salicylous acid.}}+2H_2O;\text{ and}$$

$$\overbrace{2C_7H_8O}^{\text{Saliretin.}}+O_2=\overbrace{2(HC_7H_5O_2}^{\text{Salicylous acid.}}.$$

Salicylous acid exists in nature in the flowers of the common meadow-sweet, the *spiræa ulmaria,* and may be got by distilling these flowers with water. It is generally prepared from salicin by the decomposing action of dichromate of potass. It is a colorless oily liquid, having a hot pungent taste, and the odor of the flower of the meadow-sweet. It combines with soda and potass to form salicylides. It strikes an intense violet color with ferric chloride.

If salicylous acid be fused with caustic potass, part of the hydrogen is liberated, and salicylic acid is formed:—

$$\overbrace{HC_7H_5O_2}^{\text{Salicylous acid.}}+KHO=\overbrace{KC_7H_5O_3}^{\text{Salicylate of potass.}}+H_2.$$

The same result takes place when salicylous acid is boiled in an alkaline liquid with oxide of copper.

Salicylic acid may be obtained in several ways. From salicin it may be formed by fusing it for some time with caustic potass. From the oil of winter-green it may also be formed by boiling it with caustic potass for a few minutes.

Now-a-days it is always prepared from carbolic acid by the action of caustic soda.

It occurs in needle-shaped crystals, sparingly soluble in cold, but very soluble in hot water. It combines with alkalies to form salts which are much more soluble. It gives a violet reaction with perchloride of iron.

When taken into the system, part of it passes away in the urine unchanged, and part becomes converted into salicyluric acid, a crystallizable colligated combination of glycocine, by a process analogous to that

by which, under similar circumstanees, benzoic acid is converted into hippuric acid. Salieylurie acid also gives a violet reaction with the iron salt. By boiling with concentrated hydrochloric acid, it may again be split up into salicylic acid and glycocine.[1]

It has been asserted that saliein is converted into salicylic acid in the system; and Senator of Berlin has advaneed the hypothesis that it owes its therapeutic properties to sueh eonversion.

This view has been very generally accepted.

But from what has been said as to the chemical relationship of the different salicyl compounds, it will be seen that the conversion of saliein into salicylic acid is not the simple process that some would have us believe it to be.

To be converted into salicylic aeid, salicin must be subjected to an amount of oxidizing force which is not likely to be brought to bear upon it in the system. We have already seen that boiling for a few minutes yields only saligenin; that by more prolonged boiling, saliretin is obtained; and that the action of a very powerful oxidizing agent, such as ehromic acid, is required to earry the oxidation beyond this point, and to convert salicin into salicylous acid. Even then the process has not served to produce salicylic aeid. To obtain this result, salicin must be fused for some time with a concentrated solution of three parts of caustic potass to one of saliein. Less vigorous measures lead only to the formation of saligenin, saliretin, and salieylous acid. On chemcial grounds, therefore, we should expect the oxidation of salicin in the system to result in the formation of these substances, rather than of salicylic acid.

"But," says Senator, "the observations of Latheran and Millon, and of Rankc, show that salicylic acid is so converted." I do not think they do: for the tests on which these observers relied, and which Senator regards as adequate, are not sufficient. After ingestion of salicin, they found that the urine invariably gave a violet reaction with perchloride of iron, and that crystals of what they regarded as salicylic acid were found in the urine. But neither this reaction nor the crystalline form is peculiar to salicylic acid. Salicylous acid gives the same reaction, and saligenin gives a deep blue which very closely resembles

[1] Miller's Elements of Chemistry.

it. It is not shown that the crystals which they got were not those of saligenin. Moreover, in one of his experiments, Ranke found crystals of undecomposed salicin in the urine.

Dr. Spencer[1] of Bristol analyzed 1300 c.c. of the urine of a man who had taken 120 grains of salicin. "The crystalline extract consisted of an acid body supposed to be salicylic acid along with salicyluric acid. The acids could not be separated from one another, nor the amount of each determined, as no good method of separation is known; but there was no doubt that some of the crystals contained nitrogen. Now, it may be fairly computed that the patient had taken 120 grains of salicin in the period during which the 1300 c.c. of urine were passed. 120 grains of salicin might yield, if all of it was converted into saligenin and glucose and thence into acid, 50 grains of salicylic acid. How much salicylic acid this patient excreted we cannot tell. But we know that only about 12 grains of mixed acid crystals were recovered from a quantity of urine, representing 50 grains of salicylic acid. And this 12 grains represents glycocine as well as acids."

But here, as in the experiments of the German observers, what proof have we that salicylic and salicyluric acids were excreted? It is not shown that the crystals were not saligenin; and that the nitrogen which some are said to have contained, was not derived from urea or uric acid. Moreover, supposing that the crystalline matter did consist of salicylic and salicyluric acids, what proof have we that these acids were formed in the body, and not from salicylous acid or saligenin during the process requisite to the formation of an ethereal extract? The only certain point is, that from 120 grains of salicin there was not produced enough salicylic acid to exercise any possible therapeutic effect.

The salicyl compounds are so recent an object of therapeutic interest, and the changes which any one of them undergoes in the system so little understood, that anything like dogmatic assertion should be avoided.

I do not say that salicylic acid *cannot* be formed from salicin in the system; but I do say that saligenin, saliretin, and salicylous acid, are

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[1] The Chemical and Therapeutic Relations of Salicin and Salicylic Acid, by W. H. Spencer, M.A., M.D., Senior Physician, Bristol Royal Infirmary, etc. (Transactions of Bristol Medico-Chirurgical Society, 1878.)

more likely to result from its decomposition, and serve equally well to explain those results which have been regarded as indicative of the presence of salicylic acid.

All the salicyl compounds, except salicin, give a blue or violet reaction with ferric chloride. Saligenin, saliretin, and salicylous acid are easily formed from salicin: salicylic acid with difficulty. The reaction got by adding ferric chloride to the urine of one taking salicin, is most likely due to the presence of saligenin. Even those who have tried to prove that this reaction is due to the presence of salicylic acid, have succeeded only in demonstrating that, after ingestion of salicin, that acid is not formed in quantity sufficient to produce any therapeutic effect.

Chemical evidence does not support the view that salicin is converted into salicylic acid in the system.

But the question has also a therapeutic aspect. For if it be the case, as Senator asserts, that salicin "owes its therapeutic virtues" to its conversion into salicylic acid, then ought both drugs to exercise the same action on the system. But this is in direct opposition to clinical experience; for observation shows that salicin possesses therapeutic properties not possessed by salicylic acid; and that salicylic acid gives rise to symptoms which do not follow the administration of salicin.

1. Salicin is a bitter tonic, and may be prescribed with great advantage as such. Given in the dose of ten grains three or four times a day, when the use of such a tonic is indicated, it stimulates the appetite, and produces a generally tonic action such as frequently follows the administration of quinine. In the debility of the early stage of convalescence from acute diseases, it is very useful.

Salicylic acid has no tonic action. It tends rather to produce nausea and depression.

This different effect of the two drugs is evidenced by a fact noted by observers who have used them both in the treatment of acute rheumatism—that cases treated by salicin are less debilitated at the end of the attack, and convalesce more rapidly, than those treated by salicylic acid.

2. The quantity of salicylic acid requisite to the cure of acute rheumatism often produces great disturbance of the system. This disturbance shows itself chiefly in the brain and the heart.

The brain. Numerous cases have been recorded in which the administration of salicylic acid has been followed by delirium, more or less violent. Few who have had much experience in its use can have failed to have met with this effect. Sometimes the cerebral disturbance is really alarming.

It was supposed by Murchison and others that this symptom was due to a disturbing action of the acid on the renal secretion, and consequent retention in the blood of excretory products. But that hypothesis has been set aside by the fact that delirium has been noted in cases in which there was no interference with the action of the kidneys, and no retention of excreta.

It has also been thought that this disturbance might be due to the presence of carbolic acid, consequent on imperfect purification of the drug. There is reason to believe that in some of the earlier reported cases this may have been so; but there is now no doubt that such an explanation applies only to a few; and that cerebral disturbance may be produced by salicylic acid whose purity is undoubted.

Without causing actual delirium, salicylic acid may give rise to nervous prostration, a sense of weight and oppression in the head, and a feeling of general misery which is very distressing.

Salicin gives rise to no such untoward effects. "I have never seen salicin, even when given in very large dose, produce delirium," says Dr. Sydney Ringer, who has made very extensive observations with it.

The *Lancet* for July 31, 1880, contains a clinical abstract of a half-year's hospital work by Dr. Charteris, Professor of Materia Medica at the Glasgow University, and Physician to the Glasgow Royal Infirmary.

The cases of rheumatic fever are thus referred to:—

"They were all treated with salicin in twenty-grain doses every two hours, with invariably satisfactory results. In all the cases the patient was free from pain in twenty-four hours, and the temperature was normal in forty-eight. When this result had been attained, the salicin was given in smaller doses, twenty grains every four hours for the first day, and afterwards the same quantity every six hours for two days, when it was stopped and a tonic administered. Dr. Charteris had invariably followed this line of practice for the last four years, and could not speak too highly of the remedy. He had never known it cause delirium or weakening of the heart's action. On the contrary, the relief

was marvellous and the recovery materially hastened. On an average, the patient was able to leave bed within seven days after admission, and no other treatment he had tried could give any result at all to be compared with this. In former years he had tried for comparison the salicylate of soda, but it caused temporary deafness, headache, and insomnia, and he had latterly entirely abandoned it, being more than satisfied with the action of salicin."

Dr. Flint[1] says that "salicylic acid in some instances has produced alarming toxic effects, and even death. No such effects have been observed to follow salicin; and its controlling influence over acute rheumatism is probably not less than that of the salicylic acid."

I myself have used salicin more frequently and more freely than salicylic acid, but have never found it cause delirium. I have on numerous occasions seen such disturbance produced by salicylic acid.

The only unpleasant effects which I have found follow large doses of salicin, are such tinnitus, partial deafness, and headache, as frequently result from the administration of quinine.

The heart. Symptoms of cerebral disturbance are not the only toxic effects of salicylic acid. The heart also suffers. The cardiac symptoms are much less obvious than the cerebral, and are, therefore, more apt to escape notice, unless they exist in a marked degree.

The action of salicylic acid on the heart is essentially depressing. The evidence of this is feebleness and increased frequency of the pulse and cardiac action: the sounds are wanting in tone, and the apex beat becomes less distinct. The general prostration which accompanies this condition, varies with the extent of the cardiac depression. If this is very marked, the patient's state may cause alarm and anxiety.

If there be at the same time enough cerebral disturbance to cause wandering and delirium, the patient has much the aspect of one suffering from typhoid depression.

With the omission of the drug, the normal heart regains its tone. But if the muscular substance of that organ be at all weakened or softened from other causes, such as rheumatic carditis, typhoid fever, etc., the depressing effect of the salicylic acid may be serious, and possibly hasten a fatal termination.

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[1] Practice of Medicine.

This action on the heart is not produced by salicin. I have never seen anything approaching it, even from large and frequent doses.

If further evidence were wanted to show that salicin does not owe its therapeutic effects to its conversion into salicylic acid, we should find it in the fact that when a man is suffering from the toxic effects of the acid—while he is depressed from its action, and still under its influence—salicin may be freely administered with benefit. Under its use, the depressing effects of the salicylic acid disappear. This could not be the case if the salicin owed its therapeutic virtues to its conversion into salicylic acid.

Case XX.—A man, aged 40, who had twice previously, at 20 and 26 years of age, suffered from acute rheumatism, had a third attack in June, 1878. When seen, on the 4th day of illness, both wrists and the right knee were swollen and painful; tongue furred; perspiration acid; urine high-colored and depositing urates; pulse 100; temperature 101.4°; bowels moved by medicine; heart normal. To have twenty grains of salicylate of soda every hour, till six doses have been taken, and after that, every two hours.

He began to take his medicine at noon. In the evening I was sent for to see him. He was better, so far as the rheumatic symptoms were concerned. The joints were less swollen and not so painful; the pulse was up to 120, and was small and feeble; the temperature had fallen to 99.8°. But his general condition was much changed. His wife stated that he complained of the medicine making him feel depressed and uncomfortable after the third dose, and that after the fifth he began to wander. When seen by me, after having taken in all 140 grains of the salicylate, he had the appearance of one suffering from *delirium tremens*. His expression was anxious; he was wandering and talking nonsense, fancying that there was some one under his bed, and behind the window curtains. He knew me perfectly, but, though I was quite alone, asked who that was that I had with me. He had no recollection of having seen me in the morning, and thought that I had come straight to him from Ireland, where I had been some weeks previously. The urine was high-colored, and free from albumen; he was perspiring freely. The heart's sounds were wanting in tone; there was no abnormal *bruit*.

The salicylate was omitted, and he was ordered instead, thirty grains of salicin every two hours.

On the following morning he was much better. Had wandered during the night, but fell asleep about half-past three; slept for three hours, and afterwards had short snatches. When seen at 9 a.m., was quite rational, but feeling stupid and confused. Had no recollection of having seen me yesterday evening; but quite remembered the morning visit. Pain in joints gone; pulse 100; heart's sounds improved in tone; temperature 98.5°. To have thirty grains of salicin every three hours.

He got rapidly well.

Case XXI.—A woman, aged 30, was laid up with her second attack of acute rheumatism. Right ankle and knee and left elbow swollen and painful; acid sweats; pulse 104; temperature 102.1°; heart unaffected. She was ordered twenty grains of salicylate of soda every two hours. On the following day, after having taken 180 grains of the salicylate, the rheumatism was better; the joints were less swollen and scarcely at all painful, except on firm pressure; and the temperature had fallen to 100°: but the pulse was 120, small and feeble; she complained of nausea, and a sense of misery and depression, and thought the medicine "did not suit her." The heart's impulse was barely perceptible, and the sounds wanted tone. The salicylate was omitted, and she had instead thirty grains of salicin every two hours.

On the following day it was reported that she had slept well all night, having wakened up only twice. On each occasion she took a powder. Took seven in all, equal to 210 grains of salicin. Pain gone; the joints not even tender to touch, but feeling stiff; pulse 96, of better volume; heart's sounds pretty good; temperature 98.8°. To have thirty grains of salicin every four hours. She continued to take it so for several days, and made a perfect and rapid recovery.

Case XXII.—A medical friend suffering from subacute rheumatism, asked me to see him. He had been taking salicylate of soda, which, though it did good to his rheumatism, produced cardiac depression. The following is his own statement: "Both drugs relieved the pain, tenderness, and swelling, when taken in full doses frequently

repeated. But the salicylate, which I employed first, produced some very unpleasant effects. After taking several twenty-grain doses, a copious perspiration was produced; the strength of the pulse was very distinctly diminished, while its frequency was increased; and a feeling of most uncomfortable depression, with singing in the ears, ensued. Indeed, I hardly knew whether the disease or the remedy was the preferable. Salicin, on the other hand, improved the tone of my pulse and digestion, and relieved the pains more rapidly. To my mind, one of the great merits of salicin is the absolute safety with which large doses can be taken. In the course of one period of twenty-four hours I swallowed an ounce of it with nothing but benefit."

In this case the dose of salicylate of soda was twenty grains every two hours. While suffering from the depressing effects of this, salicin was given in larger dose, with the result stated.

These are not isolated cases; but they serve as well as a dozen would, to illustrate a point of much importance in practical therapeutics—*that salicin may be freely administered while the system is still depressed from the toxic action of salicylic acid, and that under its use the rheumatic and the salicylic symptoms both disappear.*

Did salicin owe its effects to its conversion into salicylic acid, such a result would be impossible. The rheumatism would be cured, but the symptoms referable to the salicylic acid would be kept up, so long as salicin continued to be administered.

Senator recognizes the superiority of salicin over salicylic acid in this respect, and the immunity from unpleasant symptoms enjoyed by those who take it. This he endeavors to explain by supposing that only a part of the salicin is converted into salicylic acid, and that the conversion takes place slowly and gradually, so that there is not at any time in the system enough of the acid to cause its toxic effects.

But if that be so, what becomes of his theory that the therapeutic effects of salicin are due to its conversion into salicylic acid? and how is the rapid anti-rheumatic action of salicin to be explained? If that acid be formed from salicin only slowly and gradually, then salicin ought not to have the decidedly curative effect in acute rheumatism that Senator acknowledges it to possess; for salicylic acid is so rapidly eliminated from the system, that its slow and gradual formation would not suffice to keep up its therapeutic effects. The quantity of acid requisite

to the production of a decided anti-rheumatic effect is not less than that which suffices to produce its toxic effects in susceptible subjects; and yet such persons may have their rheumatism cured by large doses of salicin, without any such unpleasant symptoms as follow the use of salicylic acid. Evidence of this we have in the cases which have been given.

When once the depressing effect of the acid had been produced, a moderate dose would suffice to keep it up; but even the quantity requisite for that purpose is not to be got from the administration of salicin in even larger dose than suffices to ensure its anti-rheumatic action.

Moreover, if salicin owes its therapeutic effects solely to its conversion into salicylic acid, and if "only a part of the salicin is converted into salicylic acid," a large dose should not be more efficacious than one half the size. If when fifteen grains are administered, only ten are in a given time converted into salicylic acid, no more than ten would in the same time be so converted, if we were to give thirty; and fifteen grains would be as efficacious a dose as thirty. But that is in direct opposition to clinical experience. It is a fact that salicin given in large dose cures acute rheumatism more quickly than the same remedy given in smaller quantity.

The therapeutic evidence, even more decidedly than the chemical, is opposed to the view that salicin owes its anti-rheumatic properties to its conversion into salicylic acid.

The fact is, that this hypothesis of Senator's was advanced at a time when men's minds were in a state of excitement about the new treatment of rheumatism, and when little or nothing was known by the mass of the profession about the chemistry and therapeutics of either salicin or salicylic acid.

Men did not stay to criticise the grounds on which the hypothesis was based; but, struck by its simplicity, accepted it at once, and without hesitation, on the authority of Senator.

There is ample evidence that Senator came to too hasty a conclusion; that his hypothesis is one which cannot be maintained; and *that salicin and salicylic acid, while exercising a like action on the rheumatic poison, have an essentially different action on the system.*

The really important question for us to determine is, not so much what changes salicin and salicylic acid undergo in the system, as how

each produces its anti-rheumatic action. There is little practical good to be got from speculating on the former point: the latter is of vital importance. But in order to come to any satisfactory conclusion regarding it, it is necessary that we should have some definite idea of the nature and mode of action of the rheumatic poison. So long as we are in the dark as to the nature of the rheumatic process, it is vain to inquire how the salicyl compounds arrest its course.

But, if the views advanced in these pages be correct—if it be the case that the rheumatic poison is a minute organism, and that the salicyl compounds owe their anti-rheumatic effects to their destructive action on this poison—then the hypothesis of Senator is as unnecessary as unreliable. For if such be the mode of action of these compounds, it is evident that, while each may have a different action on the system, they may all have the same action on the rheumatic poison.

Instead of being regarded as the only salicyl compound capable of destroying the rheumatic poison, and exercising a consequent anti-rheumatic action, salicylic acid is to be looked upon as only one of a series, comprising salicin, saligenin, salicylous acid, saliretin, helicin, and many others, any one of which may have anti-rheumatic properties.

The basis of the whole series is the radicle salicyl. If any one of the series were to be indicated, on theoretical grounds, as being *the* anti-rheumatic agency *par excellence*, it would be this radicle. As a necessary consequence of such a view, all the salicyl compounds would be regarded as possessed of anti-rheumatic properties. But as the radicle salicyl has never been isolated, and cannot be obtained in a separate form, this point must continue to be matter of speculation.

My own belief is that the whole of the salicyl series is possessed of anti-rheumatic properties; and that, in this respect, no one of them is likely to have any great superiority over the others. From observations made with saligenin and salicylous acid (oleum spiræae) I feel confident that they possess this action. But the practical difficulties in the way of obtaining and administering these, are a bar to their use. Salicin and salicylic acid are the two which are at once the most easily obtained and the most convenient for administration. They are the only two which, up to this time, have been used in medicine.

It has been clearly shown that in small doses neither remedy is of much avail. To get its full beneficial effects in acute rheumatism, each

requires to be given in large and frequently repeated dose. The explanation is obvious. The rheumatic poison is a minute organism which is propagated in, and acts on, the fibrous tissues of the motor apparatus of the body. It is, of course, carried about in the blood. The salicyl compounds act by destroying this poison. For its complete destruction a certain quantity is necessary. The sooner this quantity is introduced into the blood, and so brought to bear on the poison, the more rapid will be the cure of the rheumatism. The exact quantity required for this purpose will vary in different cases, and cannot in any one be determined beforehand.

Such being the mode of action of the salicyl compounds, it is obviously of less importance to determine with how little their anti-rheumatic effects may be got, than it is to determine how much can, in a given time, be received into the system with impunity. The larger the quantity which can be brought to bear upon the rheumatic poison, the more speedy will be the arrest of the rheumatic process. To saturate the system with the remedy is, therefore, the object in view: and the question for consideration is how this saturation may be most speedily and safely accomplished—or how, in other words, the rheumatic poison may be most rapidly and effectively destroyed, without injury to the system.

Salicin and salicylic acid being the only salicyl compounds used in medicine, the question narrows itself into a consideration of the respective safety of these two drugs.

On the rheumatic poison they exercise the same destructive action. Senator, indeed, has asserted that the anti-rheumatic action of salicin is more slowly produced than that of salicylic acid. Such an opinion was the necessary outcome of his view that it owes its action to its conversion into that acid, and that such conversion is partial and slow: but this view we have seen to be untenable. In my experience, there is, in rapidity of action, very little to choose between the two. The chief question is, "Which produces its destructive action on the rheumatic poison with least disturbance of, and danger to, the system?" On this point there can be no doubt. The quantity of salicylic acid requisite to the cure of acute rheumatism, often gives rise to so much disturbance of the brain and heart, that the administration of the drug cannot be continued without risk. Such disturbance does not follow the ad-

ministration of salicin, which may be given freely, and without fear of any untoward result attributable to it. It is impossible to saturate the system with salicylic acid without risk. It may be saturated with salicin with impunity. Of how much importance it is that such saturation should be effected not only speedily, but without the production of cardiac depression, we shall see when considering the treatment of the heart complications of rheumatism.[1]

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[1] Salicin is prepared from the bark of different species of willow. The bark is removed in spring, when it contains the largest quantity of the bitter principle, so that the quantity in the market during the summer represents all that is to be had till the following spring. Previous to the publication of my original paper (March, 1876), salacin was rarely prescribed, and was kept by chemists chiefly as a curiosity. There was but a limited quantity in the market. The price at that time was two shillings an ounce. After my paper appeared it speedily rose to six, eight, and even twelve shillings; and ultimately ceased for a time to be quoted in the druggists' monthly lists. The demand far exceeded the supply; and no more bark could be had till next spring. And yet chemists continued to supply it. They could not have given pure salacin, for it was not to be had. The combination of rise in price, great demand, and insufficient supply, led to the usual result of such a combination—adulteration. The substance used for this purpose was boracic acid; and much of what was sold as salicin was, I have been informed, a mixture of boracic acid and salicin, or even of boracic acid and quinine. To this adulteration of the drug was no doubt due the unsatisfactory results which some got from it at the time to which I refer.

The following interesting letter I received from South Africa not long after the publication of my original paper on the Treatment of Acute Rheumatism by Salicin.

"*Port Elizabeth, South Africa, April 14th*, 1876.

"Dear Sir,—I have seen with much interest your papers in *The Lancet* on the Treatment of Rheumatism by Salicin, and thought that the following story might be welcome.

"In 1861, I was district medical officer in Hope Town, on the banks of the Orange River, not far from the now celebrated diamond-fields. The town is situated in one of the high plateaus of South Africa, and the country is occupied by a race of nomadic Dutch Boers, who live in waggons or tents, traveling about from place to place, as the rains, or rather occasional thunder-storms, filled the natural hollows. When these are dried up, the farmers are obliged to fix their abodes on the banks of the river.

"The temperature in summer is very high, and the dryness of the atmosphere so great that surgical instruments or fire-arms never rust. The winter, with its clear bright sun and cool temperature, is most exhilarating. You can imagine that a doctor's life in such a region must indeed be a sinecure. On one occasion, however, I was sent for to visit the wife of a Dutch Boer, who was said to be very ill. I found my patient of the usual Dutch build, *informe ingens*, lying on a camp-bed in a little tent, where the heat was something

terrific; a naked bush child trying to fan away the cloud of flies which was tormenting my poor patient, bound hand and foot, I may say every joint, in the cruel bonds of as fierce an attack of rheumatic fever as I ever saw. She was perspiring profusely. The time that has elapsed has obliterated my memory of pulse, temperature, and heart complication. I prescribed the usual alkaline mixture, with calomel and Dover's powder at bedtime, and rode away.

"Some two months after, my former patient entered my surgery, looking remarkably well, and I very naturally congratulated myself and her that she had recovered so completely. I was quite taken aback when she bluntly told me that my physic hadn't helped her a bit. On inquiring what had helped her, she said that the old Hottentot shepherd had made her a decoction of the shoots of the willows which grow on the banks of the river, and that after taking this for a few days she began to get better.

"Your papers in *The Lancet* brought the picture of the stout Dutch woman back to my memory. I afterwards learned that a decoction of willow-tops is a favorite remedy for fever, and what the Boers and native Hottentots call 'sinken kors' or rheumatic fever.

"Trusting that this remedy which you have scientifically thought out may prove as beneficial as the 'willow-tea' selected by these children of nature,

'I remain yours very truly,

"FREDK. ENSOR,

"Surgeon to Provincial Hospital, Port Elizabeth."

CHAPTER XVII.

THE TREATMENT OF VASCULO-MOTOR RHEUMATISM.

In its general pathology, rheumatism of the heart is identical with rheumatism of the joints. The poison is the same; the textures which chiefly suffer are the same; and there is no difference in the mode in which the poison acts. The morbid process is, therefore. fundamentally the same in both.

Such being the case, it is natural to suppose that both should yield to the same treatment, and that the beneficial results which follow the administration of the salicyl compounds in rheumatic inflammation of the joints, should equally follow their administration in similar inflammation of the heart. And such no doubt would be the case, if the heart were in all respects similarly situated to a joint. But it is far from being so. For though, in its general pathology, rheumatic inflammation of the former is identical with similar inflammation of the latter, there exist between them several important differences, which it is necessary for us to recognize, if we would form a just estimate of the relative value of the salicyl compounds in the treatment of each. For the formation of such an estimate, we must not only have accurate views regarding the general pathology of rheumatism, but must also be alive to the special peculiarities of the disease as it presents itself in th vasculo-motor system.

In both heart and joints it is the fibrous textures which suffer first and chiefly. In both heart and joints these textures have the same duties to perform—they regulate movement, and resist strain. The chief difference to be noted between them, is in their relative functional activity. A joint acts only occasionally, never for more than a few hours in succession, and gets complete rest for many hours every day. The heart gets no rest, but beats on by day and by night, without cessation or repose.

This physiological difference exercises a vast and important influence

in disease, and especially in such acute inflammation as that which now engages our attention.

To an inflamed organ, rest is of the utmost importance. If a joint is inflamed, it becomes painful; motion increases the pain; instinctively we give it rest, and its function is in abeyance till the inflammation is at an end. If a man suffering from rheumatic inflammation of the knees and ankles were to persist in going about as usual (supposing such a thing to be possible), he would thereby prevent recovery. The salicyl compounds might be given so as to destroy the rheumatic poison, but the continued exercise of the inflamed textures would keep up the inflammation, independently of the cause which originally set it agoing, and they would probably not recover till they got rest.

When the heart is inflamed, it gets no rest: no matter what the consequences to itself, its work has to be done; and done it is, so long as life lasts. The fever of the accompanying joint affection, as well as the inflammation of its own textures, causes increased excitability and increased frequency of action, so that, instead of rest, there is greater activity—instead of its function being in abeyance, it is exalted. This it is which makes the chief difference between the results of rheumatic inflammation of the heart, and similar inflammation of a joint; and this it is which makes the former so much less amenable to treatment.

In both heart and joints the rheumatic poison causes inflammatory thickening of the fibrous textures; but in the latter, the inflamed tissue gets rest, and the morbid change is temporary; in the former, rest is unattainable, and the morbid change is permanent. It is not in the nature of the morbid process, but in its results, that lies the difference between the two. In considering the question of their respective amenability to treatment, it is essential that this should be borne in mind, and that the effects attributable to the inflammatory process, should be distinguished from those directly due to the action of the rheumatic poison.

The destruction of the rheumatic poison *must* put a stop to its direct action on the heart as well as the joints. But to do this, is quite a different thing from removing the morbid products resulting from that action. It is a step, and a very necessary one, towards that end; but something more is requisite to its complete attainment. For this, it is requisite that the inflamed textures should have rest. In the joints

this is easily got; in the heart it is unattainable. The inflamed valves continue to be strained, their roughened surfaces continue to rub, the friction keeps up the irritation; the damage which has been done by the rheumatic poison is thus increased by some of its effects, and restoration to the normal is rendered all but impossible.

Though the heart affection very seriously complicates the rheumatic attack during whose course it occurs, it is not in any way, or in any case, to be regarded as an *accidental* complication, but always as part of the disease, and as being induced in exactly the same way as the joint inflammation.

If the heart suffer, it does so for the same reason that a given joint suffers—because its textures contain the second factor requisite to the propagation and action of the rheumatic poison. If the heart contain this second factor, it does so naturally, and before the rheumatic poison gains entrance to the system. It is, therefore, in danger from the very first: and, theoretically, there is no reason why it should not give evidence of disturbance at as early a period as the joints. Practically, there are three reasons why it should not do so:—

1. The joints are much more numerous; and the chance of one or more of them suffering first, is correspondingly great.

2. The amount of fibrous tissue in a given large joint, is much greater than that which exists in the heart. The chance of the locomotor apparatus being the first to suffer is thus increased to a corresponding degree.

3. The symptoms of rheumatic inflammation of the fibrous textures of a joint, are prominent from the commencement of the attack: those of rheumatic inflammation of the fibrous textures of the heart, are more tardily developed, and are not apparent till these textures have suffered for some time.

Let us consider this third point more carefully, for it is an important one.

In both joint and heart, the fibrous tissue is the part which suffers first. In the joint the inflammation extends from the fibrous textures to the synovial membrane; in the heart, from the fibrous rings and valves to the endo- and peri-cardium. Before the synovial membrane becomes affected, there is already pain, tenderness, and all the necessary evidence of inflammation of the fibrous textures. But, until the mis-

chief has extended to the endo- or peri-cardium, there is no such evidence, and no possibility of diagnosing the existence of inflammation of the fibrous textures of the heart; for such inflammation gives rise to no symptoms or signs before some change has taken place in one or other of these membranes.

The signs of endocarditis (to which for the present we shall confine our attention) are those of roughening of the endocardial surface of a valve; but such roughening is not produced by the direct action of the rheumatic poison on the lining membrane: it is the indirect result of a prior inflammation of the subjacent fibrous tissue.

It follows from this, that there is a stage of the endocarditis which precedes the roughening of the endocardial surface, and precedes, therefore, the earliest evidence of the heart affection. In other words, rheumatic endocarditis cannot be diagnosed till the ailment has existed for one or more days. An endocarditis whose physical signs first become apparent on a Wednesday, has almost certainly begun on Monday or Tuesday, if not sooner.

If the rheumatic poison affect a joint and the heart simultaneously, pain, the earliest evidence of joint inflammation, will precede, possibly by some days, the endocardial blow, which is the earliest indication of the heart being affected. The rapidity of development of the endocardial murmur will vary with the acuteness of the attack; but in any case, its comparatively late development will make the cardiac inflammation appear secondary to that of the joints, though the two may in reality have originated simultaneously.

Pain, the earliest and chief evidence of rheumatic arthritis, exists from the commencement of the attack; but an endocardial murmur, the most reliable, and generally the only, evidence of endocarditis, is not an early sign: it marks the attainment of that stage of the disease at which the lining membrane becomes roughened.

Thus it happens that by the time an endocarditis is diagnosed, serious damage has already been done to the heart. The roughening which produces the endocardial blow is caused by rubbing of the swollen valves: the roughening itself leads to the deposition of lymph on the affected surface, and to increase of friction. And so the mischief is kept up, independently of the action of the rheumatic poison.

When the heart suffers in acute rheumatism, it nearly always does

so at an early stage of the disease. In this respect, it resembles the joints. No matter how prolonged a rheumatic attack may be, all the joints which suffer during its course, are generally affected within the first week or ten days. Some of them may suffer more than once; but joints not affected up to that time are likely to escape altogether.

So it is with the heart. If it suffer at all, it generally does so during the course of the first week. If that is passed over in safety, the heart is likely to escape. And the reason is obvious. What renders the heart or a joint susceptible to the action of the rheumatic poison, is the presence in its textures of the second factor requisite to the propagation and action of that poison. If the heart contain this second factor at all, it does so from the commencement, and is in danger from the first moment that the poison gains entrance to the system.

The points to be chiefly borne in mind are:—

1. That the heart, if it suffer at all in acute rheumatism, suffers early.

2. That the part first affected is the fibrous structure of the rings and valves.

3. That the endo- and peri-cardium suffer secondarily, and, therefore, later.

4. That, prior to its extension to their endocardial covering, inflammation of the fibrous textures of the valves cannot be diagnosed.

5. That injury to the valves, though indirectly due to the action of the rheumatic poison, is directly and chiefly attributable to the mechanical rubbing of one part against another.

6. That roughening of the endocardial surface is developed only after the inflammation of the fibrous textures has reached a certain stage—that of thickening.

7. That such roughening is no essential part of the action of the rheumatic poison; but a change incidental to the peculiar function and construction of the affected tissues.

8. That rest to an inflamed organ is of the first importance to its recovery.

9. That this condition is unattainable in the heart.

Keeping before us these special peculiarities of rheumatic inflam-

mation of the heart, we are in a position to take up the important question of the action of the salicyl compounds in such inflammation.

The question has naturally two aspects—a prophylactic, and a curative.

1. Do the salicyl compounds tend to prevent heart complications in acute rheumatism?

2. Do they have a curative action on these after they have occurred?

We shall first deal with the prophylactic aspect of the question.

That a remedy which rapidly cures acute rheumatic inflammation of the joints, should tend to ward off, if not prevent, the heart complications which so frequently accompany such inflammation, is a reasonable supposition. And sanguine hopes were at one time entertained that such an action the salicyl compounds would have.

These hopes have not been realized. Numerous cases have been recorded in which heart complications have appeared in the course of acute rheumatism, after the salicyl treatment had been established.

How is this to be reconciled with the views advanced, first, as to the pathology of rheumatic inflammation of the heart; and, second, as to the mode of action of the salicyl compounds?

If it be the case that rheumatic inflammation of the heart is produced in the same way as rheumatic inflammation of a joint: and if it be the case that the salicyl compounds destroy the rheumatic poison, should not these compounds, in virtue of that action, ward off and arrest the course of heart inflammation, as they ward off and arrest the course of inflammation of the joints? Theoretically, yes; practically, no. And "no" for the following reasons:—

In order to get the full beneficial action of the salicyl compounds in rheumatism of the joints, they have to be given in large doses frequently repeated; and their action has to be kept up for a time after the pain is abolished and the fever allayed. In other words, the rheumatic poison has to be overwhelmed, as it were, by the agency which destroys it; and the system has to be saturated for some time with this agency to render that destruction complete. If the salicyl compounds be not given in sufficient dose, or for a sufficient length of time, a certain quantity of the poison evades destruction, and may produce mischief.

In many of the recorded cases in which heart mischief appeared

during the salicyl treatment, its occurrence was fairly attributable to the inadequate protection of a small dose. From what is observed in the joint affection, we know that frequently repeated full doses are requisite to a rapid cure, and the prevention of renewed arthritic attacks. The heart is, in this respect, in the same position as a joint, and runs the same risk of suffering while the blood contains the rheumatic poison.

But a more constant, and probably more potent agency intervenes, not actually to diminish any prophylactic action possessed by the salicyl compounds, but to render that action less apparent, and to lead us to underrate their usefulness in that respect.

We have seen that, in the heart, the rheumatic poison acts primarily on the fibrous textures of the rings and valves, and only secondarily on the lining and investing membranes. We have also seen that inflammation of these fibrous textures gives rise to no symptoms or physical signs, and that not till the membranes are affected can the disease be diagnosed. In other words, the rheumatic poison is acting on the heart for some time before there is any evidence of its doing so. The first indication of its action on the endocardium, is the development of an endocardial blow. But before this can be developed, there take place—

1. Cellular infiltration of the fibrous textures of the valve, and consequent elevation of its endocardial covering.

2. Rubbing of one segment against another.

3. Roughening of the endocardial surface consequent on such friction.

All that takes time—how much it is impossible exactly to say—but probably not less than from one to two days: so that before an endocarditis is detected, it has probably existed for at least thirty-six hours.

If the salicyl compounds be given to a man just as the fibrous textures of the heart are beginning to suffer, they are not given in time to stop the action of the rheumatic poison on them, or to prevent proliferation of their cellular elements; they are not given in time, therefore, to prevent swelling of the valves, and rubbing of their segments, and, consequently, not in time to prevent those changes on the endocardial surface which lead to the signs of endocarditis.

The development of an endocardial murmur two days after the com-

mencement of salicyl treatment, seems, on a superficial view of the matter, to indicate that this treatment possesses no power to prevent cardiac complications. More careful inquiry shows this conclusion to be hasty, and probably erroneous. For, first, the signs of endocarditis are not developed till the disease has already existed for one or two days; and, second, as we know from what is observed in rheumatic inflammation of the joints, it takes a day or two to get the full action of the salicyl compounds.

A man may begin to take these compounds on Monday, and on that day the heart's sounds may be quite normal. On Tuesday his joint inflammation may be much better; but there may be a distinct endocardial blow. That enough of the salicyl compound had been taken to check the rheumatic process, is evidenced by the improvement in the joint inflammation; that what served to allay the joint inflammation, did not suffice to save the heart, is evidenced by the development of the endocardial blow.

From the coincident decline of the arthritic, and development of the cardiac symptoms, the inference might naturally be drawn, and has in several cases been drawn, that the salicyl compounds have no power to prevent cardiac complications in rheumatism. But a careful examination of all the circumstances of the case would lead to a more cautious, if not different, conclusion.

Any prophylactic property possessed by the salicyl compounds in rheumatic inflammation of the heart, must be due to their destructive action on the rheumatic poison. They save the heart by destroying the poison. But this saving action cannot be got unless they are given in adequate quantity *before the poison has begun to act on the heart*, for with the commencement of morbid change in that organ, terminates the period of possible prevention. Inflammation of the fibrous textures of the heart exists, as we have seen, for one or two days before it can be diagnosed. It takes also from one to two days to introduce into the system enough of the salicyl compounds to destroy the rheumatic poison, and to enable us to get the benefit of the prophylactic action which such destruction implies. The rheumatic poison may have begun to act on the heart before the salicyl treatment was commenced, but its symptoms may not be developed for twenty-four hours later. The morbid process had precedence of the treatment. It had a

clear lead of twenty-four hours; and prevention was out of the question.

But even if the start were fair and equal—even if the salicyl treatment commenced at the same moment that the rheumatic poison began to act on the fibrous textures of the heart—the morbid process would still have the advantage, for probably twenty-four hours would elapse before there could be introduced into the system the quantity of the salicyl compounds requisite to the destruction of the poison. During these twenty-four hours the rheumatic poison would have time and opportunity to cause such change in the fibrous textures as would lead to thickening of the valves, to consequent friction of their segments, and to the development of the symptoms of endocarditis; while the continued activity of the inflamed tissues would prevent the decline of the inflammation, which might otherwise be expected to follow the destruction of the rheumatic poison.

It is impossible to state with exactitude, either the time which, in a given case, must elapse between the commencement of cardiac inflammation and the development of an endocardial blow, or the quantity of the salicyl compounds requisite to destroy the rheumatic poison. The former must vary with the acuteness of the attack; the latter with the amount of poison in the system at the commencement of treatment, and with the stage of the disease at which treatment commences.

In no given case can we positively assert that the absence of heart complications is due to the preventive action of the salicyl compounds. All that we can do is to satisfy ourselves, first, as to the mode in which the heart complications are brought about; and, second, as to the manner in which the salicyl compounds act. Having done this, we are in a position to judge as to whether or not they are likely to possess any prophylactic properties.

It has been abundantly proved that the salicyl compounds do possess the power of arresting and cutting short the course of rheumatic fever. This means that they possess the power, not only to allay the inflammation which already exists, but also to prevent that which would certainly arise, either in those joints which have already been affected, or in others, if the attack were prolonged. If we admit their power to prevent rheumatic inflammation of the joints, we must also admit their power to prevent similar inflammation of the heart.

If the view which has been advanced as to their mode of action be correct, they cannot fail to prevent cardiac complications, *if only they are given in sufficient quantity to destroy the rheumatic poison before this has begun to affect the heart.*

The chief obstacle to their doing so, is the early stage at which the hear is apt to suffer. It is only in a minority of cases that time and opportunity are given to get the full action of the salicyl compounds, before the heart is affected. This is specially the cases in hospital practice, in which the patients seldom come under notice before the disease has existed for the best part of a week.

The very acute cases which come under observation during the first two or three days of the illness, are also the ones in which the heart is apt to be affected from the commencement. In such cases, the joint and heart affection are often contemporaneous; though, for reasons already given, the symptoms of the latter are more slowly developed.

In subacute cases, the symptoms are developed less rapidly, and the heart affection is more likely to be delayed a few days; but so also is the period at which treatment commences, for such cases are generally ailing for at least three or four days before they come under notice.

In acute cases, the heart affection is developed so soon, and so quickly, that there is no time to get the prophylactic action of the salicyl compounds. Subacute cases come under notice at so comparatively late a period, that there is no opportunity to do so.

So that, whatever prophylactic properties we may accord to the salicyl compounds on theoretic grounds, there remains the difficulty that in actual practice this result is seldom attainable. All that we can say is, that it may be got in some cases; but in no given case can we be sure of having got it.

With such a possibility before us, however; and with such a tremendous issue at stake, it is impossible to exaggerate the importance of the early and free administration of the salicyl compounds in all cases of acute and subacute rheumatism; for we never know when we may be dealing with a case in which prophylaxis is attainable. The bare possibility of such a result is worth striving for. But promptitude and decision are requisite to success. A halting spirit, and inadequate dose, court failure. At least thirty grains should be given every hour till there is decided evidence of action, and then the dose should be

diminished slowly. A delay of a few hours in commencing treatment, or the administration of the drug in insufficient dose, may make all the difference between perfect recovery and recovery with a damaged heart—a calamity which, in some cases, is scarcely preferable to death, so hard may be the conditions under which life is carried on.

Do the salicyl compounds have a curative action in rheumatic inflammation of the heart?

Regarding such inflammation as identical in nature and pathology with rheumatic inflammation of the joints; and recognizing the distinctly curative effect of the salicyl compounds in the latter, it might, not without reason, be expected that they should have the same action in the former—that they should cure rheumatic carditis, as they do rheumatic arthritis. Experience, however, has shown that such is not the case; and that under the salicyl treatment, as under all others, rheumatic endocarditis (to which we shall still confine our attention) generally, if not always, leads to permanent damage.

Attention has already been drawn to one obstacle which intervenes to make the treatment and cure of inflammation of the heart specially difficult—the impossibility of giving rest to the inflamed textures. This is an obstacle which no treatment can overcome. It is an important factor in keeping up the mischief originated by the rheumatic poison, and affords an adequate explanation of the fact, that the treatment which allays acute rheumatic inflammation of a joint, may fail to have a like action in similar inflammation of the heart. In both, rest is essential to quick recovery. In the one it is easily obtained; in the other it is unattainable.

But it is not enough to explain why the ailment should be so little amenable to treatment during its acute stage. We have also to account for the permanent duration of the endocardial mischief.

Pericarditis may be perfectly recovered from, the effused products may be absorbed, and the membrane restored to its natural state. So, too, may myocarditis. But we cannot say the same of endocarditis. Its signs persist after all inflammatory mischief has ceased. It is a pathological fact, that when once a certain amount of change has taken place on the endocardial surface, the damage is irremediable and permanent. The endocardium is the only structure habitually affected

by the rheumatic poison, of which this can be said. The fact demands, and admits of, explanation.

The endocardium is the only structure in the heart which has no analogue, anatomical or physiological, in the joints. The fibrous and muscular textures of the heart and joints have a like structure and function. So have the pericardial and synovial membranes. The endocardium alone is unrepresented in the loco-motor apparatus. It stands alone, too, in its pathology. Its scanty vascularity, and low vital activity, make it insusceptible to acute general inflammation; such inflammation is, therefore, unknown in connection with it.

The same circumstances also intervene to prevent the absorption of products effused on its valvular portion during an attack of rheumatic endocarditis. To the absorption of such products a certain degree of vascularity is necessary: such vascularity does not exist in the endocardium; and, therefore, lymph deposited on its surface is not absorbed.

It may, indeed, be said that a degree of vascularity which suffices for the effusion of lymph, should suffice also for its absorption. But the lymph deposited on the valves during rheumatic endocarditis is not all effused. Great part of it is deposited directly from the blood, on the roughened surface; and even this primary roughening results from irritation caused, not directly by the rheumatic poison, but by friction of the valvular surfaces, produced in the manner already explained—a mechanical force which, in the case of the heart, cannot be equalled or counterbalanced by any agency which stimulates absorption. The only force which could have this effect is occasional pressure; and that is not available.

It is evident that the condition is one on which medicinal treatment can have no effect; and thus is explained the inability of the salicyl compounds to repair the damage done during an attack of rheumatic endocarditis.

The direct cause of all the objective, and most of the subjective, symptoms of endocarditis, is not the rheumatic poison which causes the inflammation—it is not even the inflammation itself,—it is the physical change caused by the rubbing and roughening of the swollen valves. The lymph deposited during rheumatic inflammation of the heart, differs in no respect from that thrown out during non-rheumatic

inflammation. No one would expect the salicyl compounds to remove the latter. It would be as unreasonable to expect them to remove the former. These drugs are not deobstruent, they are anti-rheumatic. They cure rheumatic fever; but they do not stimulate absorbents, or remove effused products.

The fact that the salicyl compounds are powerless to remove cardiac damage, is an urgent reason for getting the system under their influence and out of that of the rheumatic poison, before the heart becomes involved.

But though they fail to effect a cure, it cannot be said that these compounds are totally without influence in cardiac inflammation. For if their action on the rheumatic poison be such as we suppose, they cannot fail to be of some benefit. If they destroy the rheumatic poison, they must, by so doing, curtail the duration, and limit the extent, of its action on the heart, and so mitigate the severity of the cardiac mischief.

It is, of course, impossible to demonstrate, in any given case, that the heart inflammation has been allayed by the treatment; for the disease does not tend to death in more than a minority of cases. But it is equally impossible not to see that, in some cases, the salicyl treatment must tend to mitigate the severity of the heart inflammation, and to some extent allay the cardiac disturbance. The following case will serve to illustrate this. It is the same patient as Case VI., already given. It was formerly instanced as evidence of the beneficial action of salicin in the joint inflammation; it is now given in illustration of its action in rheumatic inflammation of the heart.

A previously healthy girl, aged sixteen, was seen on the third day of a severe attack of acute rheumatism. She was in bed, unable to move, and actually screaming from the violence of the joint pains. The back, shoulders, elbows, wrists, knees and ankles were all the seat of severe pain; and the joints were so exquisitely tender that the least touch or movement of the bed caused her to scream with agony. The skin was hot, not perspiring; the tongue moist and furred; the urine scanty, high colored, and loaded with pink urates. The pulse was 112; respirations 20; the temperature 103.8°. There was no pain or uneasiness in the chest; but there was a soft blowing murmur with the

first sound, loudest at the apex, but audible over the whole heart. She had fifteen grains of salicin every hour for three hours, and then fifteen grains every two hours.

She wandered a little during the night, but had occasional snatches of sleep.

On the following day (the 17th April), after 120 grains of salicin had been taken, she felt much better, though still in pain; she could move the right leg a little, and allowed the joints to be pretty firmly grasped without complaining. On the previous day the least touch made her scream. The skin was covered with acid perspiration. The pulse was 96; respirations 26; temperature 102.8°. The cardiac blow was softer in character, and preceded as well as accompanied the first sound at apex; it was less distinct over body of heart.

On the 18th, after 270 grains of salicin had been taken, she felt quite well; had no pain, and could move the limbs freely without any other sensation than some degree of stiffness of the joints. The pulse was 72, very feeble; respirations 20; temperature 99.6. The heart's action was irregular; the murmur had lost its systolic character, and was now short and purely præsystolic, distinct at apex, but not audible an inch from it.

On the 19th, after having had 405 grains of salicin, the pulse was 70, the respirations 20, and the temperature 98.2°. The girl felt perfectly well. She had no subjective symptom of heart disease, but the præsystolic murmur remained, and there was some irregularity of the heart's action.

This was a very severe attack of acute rheumatism. When first seen, on the third day of her illness, the heart and all the large joints were the seat of acute inflammation, she was screaming with agony, and the temperature was 103.8°, more than five degrees above the normal. Within forty-eight hours, she felt quite well, was entirely free from pain, and the temperature had fallen more than four degrees.

That the salicin cured the joint affection there can be no doubt. It did so by destroying the rheumatic poison. For reasons already given, it could not exercise the same curative effect on the heart inflammation. But that it served to mitigate its severity there can be no reasonable doubt. Indeed, a careful consideration of the matter tends to show that such could not fail to be its action. For if it destroyed the

rheumatic poison, it must almost certainly have had a beneficial effect on the inflammation to which that poison gave rise in the heart.

But this is not the only way in which it tended to mitigate the severity of the heart affection. Under its influence the joint inflammation subsided, and the febrile disturbance came speedily to an end. This result was accompanied by greatly diminished frequency of the heart's action. As a matter of fact, the cardiac pulsations fell in thirty-six hours from 112 to 72—a fall of 40 a minute, 2400 an hour, or 57,600 a day. It is needless to point out, that this diminished frequency of the heart's action implied decreased functional activity of the inflamed textures; and that such decreased functional activity is the one condition which is most desired, and most difficult to attain, in the treatment of cardiac inflammation.

Had the rheumatic process not been cut short by the salicin, the rheumatic poison would probably have continued to act for some weeks; the pulse would have continued to beat at the rate of 112 per minute, if not more; the inflamed valves would have been every day subjected to the strain involved in their action 57,600 times more frequently than was the case. At the end of a week they would have been strained 1,128,960 times, instead of only 725,760; that is, 403,200 times more frequently—an enormous difference, which could not fail to tell on the morbid process.

It is evident from this, that independently of the good which may have resulted from the destruction of the rheumatic poison, benefit must have accrued to the heart from the diminished frequency of its action, consequent on the arrest of the joint inflammation and accompanying fever.

The disappearance of the systolic blow when the system was brought under the influence of the salicin, is a noteworthy fact. It may have been brought about in one of two ways: either the morbid change which gave rise to it was removed; or there was so small a quantity of lymph effused that the quieting of the heart's action, by permitting of the more deliberate closure of the valves, led to less strain, less forcible closure and contact of the segments, and so to diminution of friction, and consequent repair. The continuance of the præsystolic blow would seem to indicate that the latter was the true reason for its disappearance. Whichever view we adopt, the fact remains that the

systolic blow disappeared about the time that the anti-rheumatic effect of the salicin was got. So rare is the disappearance of such a sign, that one cannot fail to see a possible connection between it and the coincident decline of the joint inflammation; and to connect both with the action of the salicin.

Had the rheumatic symptoms continued, and had the heart gone on beating at the rate of 112 per minute, it is in the highest degree probable that the damage to the valve would have increased, that the surface would have become more roughened, that the blood would have continued to regurgitate into the auricle, and that this condition would have been permanent. From this disastrous result the girl was probably saved by the salicin.

The general conclusion to which we have come is, that the early and free administration of the salicyl compounds holds out the best chance, both of saving the heart from the action of the rheumatic poison, and of mitigating the severity of that action, when it is too late to prevent it; but that these compounds are powerless to remove effused products, after the heart mischief is fully established.

The general treatment applicable to rheumatic inflammation of the heart, is thus the same as that which is applicable to similar inflammation of the joints. The existence of heart complication in a case of acute rheumatism, is not only no reason for omitting the salicyl compounds, but is an additional one for giving them freely, and in large dose.

In the great majority of cases no other treatment is required. But every now and then a case occurs in which considerable benefit is got from the adoption of local measures.

In pericarditis especially, local treatment is sometimes of much importance. In the early stage of a severe attack, when pain is a prominent symptom, when the heart's action is disturbed and tumultuous, and when there is evidence of serious interference with the circulation, much good may be got by abstracting a few ounces of blood. This may be done by opening a vein, or by the application of leeches, or cupping glasses, over the region of the heart. If the symptoms are urgent, venesection affords the most speedy relief; but to do good, it must be had recourse to at an early stage. The cases are few, however, in which the desired effect may not be got from leeches.

In entertaining the question of bleeding, local or general, it must be borne in mind that the acute stage, when got over, is followed by one in which there is apt to be considerable depression and debility. If bleeding be had recourse to unnecessarily, or too freely, this stage will be rendered more marked and prolonged. The mere existence of acute pericarditis is not a reason for taking blood; such a measure is to be regarded only as the best means of allaying the urgent symptoms of the first stage of a very acute attack.

Cold, as got by the application of an ice-bag over the region of the heart, may be of benefit at this stage. It is to be prescribed only during the acute stage. In milder cases warm poultices often give relief.

After the acute stage has been subdued there is generally, especially in severe cases which have required active treatment, some effusion of fluid into the pericardium. In most cases this disappears as convalescence advances and strength returns. But occasionally it is necessary to adopt measures for its removal.

Blisters repeatedly applied over the heart, and the internal administration of deobstruents, such as mercury and iodide of potassium, are the remedies usually recommended. Blisters are certainly of use; but the debilitated condition of the patient, and the weakened state of the cardiac muscles, which suffer more or less in acute cases, indicate the use of good food and tonics.

If these measures fail, and especially if the quantity of fluid be so great as to cause serious inconvenience, it may be necessary to have recourse to tapping. The trocar of an aspirator may be introduced into the distended sac without difficulty. The best point for its insertion is the fifth intercostal space, to the left of the sternum, care being taken to avoid the line of the internal mammary artery. Whether or not the operation may be ultimately successful, it always affords relief for the time. But the operation is one which is rarely called for.

In endocarditis it is very questionable if local measures ever do good. If the case is very acute, and accompanied by evidence of distress, a few leeches may be applied. But all depletory measures should be used with extreme caution. So, too, they should in myocarditis.

There is no especial treatment applicable to myocarditis: it is

essentially symptomatic. But, as a rule, the treatment of the acute stage is the same as that of endocarditis. When that stage passes off, the administration of tonics is called for.

Attention has already been drawn to the change in the cardiac walls induced by inflammation. They become abnormally soft and weak. It is at all times of importance that the occurrence of such a change should be recognised. It is specially so in connection with the salicyl treatment.

When considering the respective merits of salicin and salicylic acid, we saw that the latter had for one of its drawbacks a depressing action on the heart, evidenced by feebleness and, generally, increased rapidity of its action; and one or two cases were instanced to show, not only that salicylic acid produced this effect, but that no such inconvenience attended the use of salicin.

In the treatment of the heart complications of acute rheumatism, it is of importance that this action of salicylic acid should be borne in mind. If there is any reason to suspect the existence of inflammatory softening of the walls of the heart, salicylic acid, if given at all, should have its action on the heart watched very narrowly. If there is any evidence of the existence of myocarditis, or of feeble cardiac action, it should not be given at all; for the addition to the already existing enfeeblement, of such depression as salicylic acid may cause, might add seriously to the patient's danger. It is not in every case that salicylic acid has an enfeebling action on the heart; but one never knows when such a case may occur. To give a remedy which may have such an action, in an ailment in which cardiac enfeeblement is the special danger with which we have to deal, is a practice which one cannot but condemn, for it cannot fail at times to produce injurious results. Fortunately it is a practice which is never called for, even in the interests of the joints; for we have in salicin a remedy which, as an anti-rheumatic, is as potent as salicylic acid; and which possesses over that acid the enormous advantage of having no depressing action on the heart.

In all cases of recent inflammation of the heart, the muscular substance is liable to be affected. In all cases in which it is affected there is produced a soft and enfeebled condition of the ventricular walls. In

all such cases the administration of salicylic acid is attended with appreciable risk.

Rest, quiet, good food, tonics, and stimulants in moderate quantity, are the remedial agencies to which we must trust in the treatment of this softened condition of the heart's walls.

The ailment is one which nearly always occurs in young people; at an age, that is, at which the system possesses great recuperative powers. If not fatal in the acute stage, recovery is generally perfect. Attention has already been drawn to the fact that it may cause sudden death. The risk of such an accident would be increased by the depressing action of salicylic acid.

CHAPTER XVIII.

CEREBRAL RHEUMATISM.

It was at one time believed that head symptoms occurring in the course of acute rheumatism were symptomatic of inflammation of the membranes of the brain. This inflammation was looked upon as due to metastasis—to a retrocession of the rheumatic disturbance from the joints to the brain. And there are on record one or two cases in which there was found, after death, distinct evidence of inflammatory change in the cerebral membranes.

But as observations increased, and *post-mortem* evidence accumulated, it was found that, in the majority of cases of acute rheumatism which proved fatal apparently by head symptoms, the brain and its membranes were normal in appearance, and gave no evidence of inflammatory disturbance.

In several cases in which these symptoms were prominent, and in which the fatal result was attributed to intra-cranial mischief, the only evidence of inflammation was found in the heart and pericardium. From this the conclusion was drawn, that cerebral disturbance occurring in acute rheumatism, was symptomatic of inflammation about the heart. This conclusion, though quite accurate in some cases, is not applicable to all; for there have been recorded not a few fatal cases of acute rheumatism, in which the head symptoms were marked during life, but in which no *post-mortem* evidence of inflammatory mischief could be found in heart, brain, or any internal organ. Of late years, clinical observation, though it cannot be said to have much advanced our knowledge of the pathology of these cases, has thrown considerable light on their symptomatology. The introduction of the thermometer, as a means of clinical research, has shown that some cases of acute rheumatism which are characterized by the occurrence of head symptoms, rapid failure of strength, and a speedily fatal termination, have also for one of their most striking peculiarities, a rapid and great rise of temperature. Instead of ranging from 101° to 103° or 104°, it

rapidly runs up to 106°, 108°, 110°, or even more. So characteristic is this range in connection with such symptoms, that the condition is now generally referred to as one of "rheumatic hyperpyrexia."

Head symptoms thus occur in acute rheumatism under three different conditions:—

1. As a symptom of inflammation of the membranes of the brain.

2. As a symptom of inflammation of the substance, or membranes, of the heart.

3. In connection with very high temperature of the body.

We shall consider each separately.

1. Rheumatic Meningitis.

There are recorded a few cases of acute rheumatism, in which the occurrence of marked head symptoms during life, and the presence of lymph, and even pus, on the surface of the brain after death, show that meningeal inflammation may occur in the course of that disease. But meningitis, occurring in the course of acute rheumatism, is not necessarily of rheumatic origin. The extreme rarity of such cases, indeed, suggests a grave doubt whether, in the few cases in which it did occur, the meningeal mischief was not an accidental complication, due to the action of some other agency than the rheumatic poison. Certain it is, that the very small proportion of cases in which such a complication occurs, detracts from the interest and importance which would otherwise attach to it; and leads to the practical conclusion that, of all possible causes of head symptoms occurring in the course of acute rheumatism, inflammation of the membranes of the brain is the least likely to be the one with which, in a given case, we have to deal.

The symptoms to which such inflammation would give rise, would not differ from those of similar inflammation occurring independently of rheumatism. Its treatment, too, would be the same, except that appropriate anti-rheumatic remedies would be conjoined with the measures specially suited to the local head affection.

2. The Nervous Symptoms of Carditis.

To the occurrence of head symptoms in connection with inflammation of the heart and its membranes, attention has already been directed, and two cases (Cases I. and II.) have been given in which all the symp-

toms during life pointed to inflammatory mischief within the cranium, but in which, after death, there was found nothing abnormal within the head, but only the indications of inflammation of the heart and its investing membrane. Since these cases were recorded, much attention has been given to this subject, and the observations of Bouillaud,[1] Macleod,[2] Hawkins,[3] Bright,[4] Burrows,[5] Latham,[6] Fuller,[7] Watson,[8] and others, have demonstrated that inflammation of the heart and its membranes, is a frequent cause of head symptoms in acute rheumatism.

It is chiefly in connection with pericarditis that they have been noted. This is probably due to its greater frequency, and more easy diagnosis, as compared with myocarditis. In simple endocarditis, head symptoms are rarely noted.

But symptoms directly referable to the brain, such as delirium and coma are not the only nervous symptoms which may occur in connection with cardiac inflammation. Sir George Burrows[9] states that "there is scarcely an affection of the cerebro-spinal system which may not be simulated by inflammatory disease of the heart and its membranes." He gives five different classes of cases: "(1) cases which were marked with all the usual symptoms of inflammation of the brain and its membranes; (2) cases simulating mania and dementia; (3) cases characterized by apoplectic and epileptic symptoms; (4) cases with well-marked symptoms of tetanus and trismus; and (5) others still more numerous, accompanied by symptoms of aggravated chorea and hysteria."

How are these symptoms to be accounted for? Nervous symptoms occurring in connection with inflammation of the brain admit of easy explanation. It is otherwise with those occurring in connection with inflammation of the heart and its membranes.

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[1] Bouillaud, Traité sur les Maladies du Cœur.
[2] Macleod, On Rheumatism.
[3] Hawkins, Lectures on Rheumatism.
[4] Bright, Medico-Chirurgical Transactions, Vol. XXII.
[5] Burrows, On Disorders of the Cerebral Circulation.
[6] Latham, Lectures on Diseases of the Heart.
[7] Fuller, On Rheumatism.
[8] Watson, Practice of Medicine.
[9] Burrows, op. cit., p. 185.

Various hypotheses have been advanced as to their mode of production.

1. They have been attributed to a vitiated state of the blood. "A distempered condition of the blood I conceive to be the true proximate cause of the sensorial disturbance occasionally observed in the course of acute rheumatism," says Fuller.[1] "Those remarkable cerebral affections—the wild delirium and violent mania—which not unfrequently occur in the course of rheumatic fever, or follow in its train, and which have usually manifested themselves along with the cardiac complication, causing doubt and perplexity in the mind of the physician as to the real organ affected, and the true nature of the disease, are to be explained by the morbid condition of the blood which is admitted to exist in the rheumatic constitution." So wrote Begbie,[2] the distinguished father of him to whose memory this book is dedicated.

But if this morbid condition of the blood sufficed for their production, such nervous symptoms would be common in rheumatic fever. Instead of occurring only in rare and exceptional cases, they would be the rule; and delirium would be as characteristic a feature of rheumatic, as it is of typhus fever.

2. They have been ascribed by some to the action of the rheumatic poison on the cerebro-spinal membranes. But if that were their mode of production, we should find in fatal cases *post-mortem* evidence of such an action. The local effects of the action of the rheumatic poison, as they present themselves in acute rheumatism (and it is only in the acute form of the disease that such nervous symptoms as we are considering occur), are essentially inflammatory; and we recognize no other direct effects in connection with its action. If the nervous symptoms resulted from the action of the rheumatic poison on the nervous centres, we should have evidence of inflammatory disturbance at the seat of its action. But the absence of such evidence is the special peculiarity of the cases which we are now considering. We cannot, therefore, look to the *direct* action of the rheumatic poison for the explanation of their nervous symptoms.

3. By others they have been attributed to metastasis—to a retroces-

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[1] Fuller, op. cit., p. 289.

[2] Contribution to Practical Medicine, by James Begbie, M.D., F.R.S.E., p. 85. 1862.

sion of rheumatic inflammation from the joints to the nervous centres. But the results of metastatic, would not differ from those of non-metastatic, inflammation; for, so far as its local effects are concerned, it would not matter whether inflammation went to the nervous centres from the joints, or originated in them independently of any prior joint affection. As it is the absence of local inflammation in the nervous centres that constitutes the peculiarity of these cases, it is evident that we cannot look to metastasis for the explanation of their peculiar symptoms.

Bouillaud thought that nervous symptoms were most apt to occur in cases of pericarditis which were complicated with pleuritis, and especially in those in which the diaphragmatic portion of the pleura was affected.

Dr. Bright, in discussing the inter-relationship of rheumatism and chorea, expressed the opinion that though the cerebro-spinal coverings were sometimes implicated, "yet the much more frequent cause of chorea in conjunction with rheumatism is inflammation of the pericardium. The irritation is probably conveyed thence to the spine; just as the irritation of other parts, as of the bowels, the gums, or the uterus, is communicated, and produces the same diseases." He further made the definite suggestion that the phrenic nerve was the "immediate means of communicating the irritation to the spinal cord."

The similarity between the views of Bouillaud and of Bright is apparent. But though their explanation might apply to some cases, it cannot be accepted for all. For, as pointed out by Burrows, rheumatic pericarditis may be complicated with pleurisy, without giving rise to nervous symptoms; and such symptoms may be marked in cases of pericarditis in which there is no affection of the pleura. In one of the most acute cases of rheumatic pericarditis which I ever saw, occurring in a previously healthy and robust woman, twenty-seven years of age; and in which, after death, both layers of the pericardium, and the whole diaphragmatic and corresponding pulmonic surface of the left pleura, were found covered with recently effused lymph, there were during life no nervous symptoms, but only those of cardiac and pulmonary embarrassment.

4. Recognizing the insufficiency of the above hypotheses to account

for the nervous phenomena with which we are dealing, Sir Thomas Watson[1] thought they might be due to disturbance of the cerebral circulation, resulting from embarrassment of the heart's action. The objections to this view are (1) that the delirium may be violent from the very commencement, and before there is any evidence of heart affection; and (2) that the cases in which nervous symptoms are most marked, are not, as a rule, those in which evidence of cardiac embarrassment occurs; but, on the contrary, those in which there are no subjective symptoms of heart disturbance, and nothing to direct special attention to that organ. Moreover, similar nervous symptoms may occur in connection with inflammation of the lung or pleura, without any inflammation of the heart or its membranes.

Clouston was inclined to attribute the symptoms in two cases of "rheumatic insanity" to rheumatic inflammation of the connective tissue of the cerebro-spinal centres. But he brings forward no pathological evidence in support of this view.

Such are the various hypotheses.

In discussing the pathology of nervous symptoms occurring in connection with rheumatism, it seems to me that error has arisen from not sufficiently discriminating between their various forms; and from regarding all nervous symptoms, no matter how different, as having a like causation. The alarming and the trivial have been slumped together, and one narrow pathological view advanced for their common explanation.

It is surely unreasonable to regard such alarming head symptoms as those noted in Cases I. and II., occurring in the course of such a formidable disease as acute inflammation of the heart, as due to the operation of the same cause, and produced in the same way, as the comparatively trivial muscular twitchings noted in cases of rheumatic chorea. And yet that is what has been done.

This manifest source of error we shall avoid by according to each a separate consideration.

The subject of rheumatic chorea we shall take up after we have discussed the pathology of the nervous symptoms now before us—those

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[1] Watson, Practice of Medicine.

[2] Journal of Mental Science, July, 1870.

noted in connection with acute inflammation of the heart and pericardium.

In studying the pathology, and mode of production, of these symptoms, three possible causes have to be considered:—

1. The morbid condition of the blood, characteristic of rheumatism.

2. The cardiac inflammation.

3. The nervous constitution of the patient.

Hitherto, attention has been directed to the first two; and but little heed paid to the third. This third seems to me to be the most important factor of all.

It is only in exceptional cases of pericarditis that nervous symptoms occur. An exceptional symptom results from an exceptional cause, and calls for an exceptional explanation. The rheumatic constitution, and the inflammation, operate in every case of rheumatic pericarditis. Of the three possible factors, the nervous constitution of the individual is the only one which can be exceptional. It is, therefore, the one which is most likely to give rise to exceptional symptoms.

In all acute febrile ailments, nervous symptoms are apt to occur. Those in whom they are most likely to declare themselves, are persons of susceptible and delicate nervous organization. They are, therefore, more common in women than in men; in young people than in those of more mature years, and in those who have already suffered from nervous disturbance than in those who have not so suffered.

Now, in looking over the recorded cases in which nervous symptoms have occurred in connection with pericarditis, it is found that they have nearly all occurred in women and boys, and that the few adult males who thus suffered had already been the victims of some abnormal condition of the nervous system. Of the sixteen cases collected by Burrows, for instance, nine occurred in females, and seven in males; but of the males, only two were over twenty-one years of age; and of these two one was a man of intemperate habits, and the other "suffered from asthma, sleepless nights, cough and expectoration, and at the same time from spasmodic contractions of the muscles of the extremities." What determined the prominence of the nervous symptoms in these cases, was not the rheumatic constitution, and not the

inflammatory nature of the case, but the special susceptibility of the nervous systems of those in whom that inflammation occurred.

In his remarks on Case I., already quoted, Andral says, "Qu'en raison des susceptibilités individuelles, il n'est point d'organ dont la lésion ne puisse déterminer les symptômes nerveux les plus variés, de manière à produire sympathetiquement les différens états morbides dont on place le siége dans les centres nerveux et leurs dépendances."

It is this individual susceptibility that forms the important feature of the cases whose peculiar symptoms we are endeavoring to explain, and it is the non-recognition of this factor that makes the explanations hitherto given of these symptoms, so unsatisfactory and inadequate.

Head symptoms occurring in connection with acute myocarditis and pericarditis, we regard as exceptional, as indicative of an unusually susceptible nervous system, rather than of any peculiarity of the disease, and as owning a pathology, and mode of production, differing in no material respect from those of like symptoms as they occasionally occur in connection with pneumonia, pleurisy, and other acute inflammatory disorders.

But though thus insisting on the importance of constitutional susceptibility as a predisposing and determining cause, due importance must also be attached to that which is to be regarded as the direct exciting cause of the disturbance—the inflammation; and there is probably some truth in the statement of Bouillaud, that the more extensive the local inflammation, the more likely is the nervous system to be affected.

From what has been said, it will be seen that the rheumatic aspect of the case is not regarded as of importance. I do not think that it has much to do with the production of the symptoms which we have been considering, the head symptoms which occur in some cases of myocarditis and pericarditis.

It is the acute inflammation of the heart, or of its investing membrane, that is to be looked to as the exciting cause of the disturbance. Such inflammation rarely occurs except in connection with rheumatic fever, and hence, such nervous symptoms as accompany it are equally rare except in connection with that disease. That it is with the in-

flammation, and not with the rheumatism, that they have a causal connection, is evidenced by the fact that they do occur in the rarer non-rheumatic, as well as in the more common rheumatic, forms of cardiac inflammation. "Of the sixteen cases I have narrated," says Burrows, "no rheumatic affection could be discovered in seven of them."

CHAPTER XIX.

THE RELATION OF RHEUMATISM AND CHOREA.

Of the existence of some relation between rheumatism and chorea, there can be no doubt. The observations of Bright,[1] Begbie,[2] Hughes,[3] Burton Brown,[4] Sée,[5] Roger,[6] and others, have placed this beyond doubt. Their evidence need not be reproduced here.

What we have to do, is to consider the nature of this relation, and the bearing of the rheumatic constitution on the choreic symptoms. It is necessary to do so, for no theory of rheumatism can be regarded as satisfactory which does not recognize, and at least coincide with, this relationship; and no view of the nature of the rheumatic constitution can be accepted as valid which does not consist with its existence.

Chorea is essentially a disease of the nervous system. Its characteristic symptom is irregular and uncontrollable muscular twitching and jerking.

For the explanation of such a symptom we turn, not to that part of the nervous centres whose derangement causes delirium, wandering, and such phenomena as were noted in connection with inflammation of the heart, but to that part of them whose function it is to initiate, control, and regulate movement—the motor centres. How the rheumatic constitution leads to disturbance of these centres, is the question which we have to solve.

There are two views on this point: one that the choreic symptoms result directly from the disturbing action on the nervous centres of the vitiated blood; the other that they are directly due to a prior affection of the heart—the rheumatic condition acting only indirectly through this.

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[1] Medico-Chirurgical Transactions, Vol. XXII.
[2] Begbie, op. cit.
[3] Hughes, Guy's Hospital Reports, 1846.
[4] Burton Brown, Guy's Hospital Reports, 1856.
[5] Mémoires de l'Académie de Médecine, Vol. XV., 1850.
[6] Archives Générales, Vol. II., 1866, and Vol. I., 1867.

The former view is that advocated by Begbie. "I cannot help coming to the conclusion that the simple and true view of the relation of rheumatism and chorea is to be found in the morbid condition of the blood, which is admitted to exist in the rheumatic constitution, and this explanation will apply equally to chorea occurring in individuals or families inheriting the rheumatic diathesis; to chorea occurring in connection with rheumatism, but without the cardiac complication, and to chorea associated with pericarditis, or endocarditis, or both—the inflammatory affections of the fibrous tissues, as well as the spasmodic affection of the muscles, and the derangement of the nervous system, originating in the same specific disorder of the circulating fluids."[1] To this explanation of the choreic symptoms, there is the same objection that applied to a like mode of accounting for the nervous symptoms noted in pericarditis. If due to the morbid condition of the blood, they ought to be much more common than they are, for that is a cause which operates in every case of rheumatism. Occurring, as they do, only in exceptional cases, they are more likely to result from an exceptional cause, than from one which operates so generally.

The view that the chorea is consequent on a prior inflammation of the membranes of the heart, is that which has commended itself to most other observers. There is some variety of opinion, however, as to the sequence of events by which the one phenomenon leads to the other.

Reference has already been made to the opinion of Bright, that the choreic symptoms resulted from irritation transmitted from an inflamed pericardium or pleura along the phrenic nerve. This explanation might apply to cases of chorea occurring in connection with pericarditis or pleuritis, but is quite inapplicable to the numerous cases in which no such inflammation exists.

In more recent times the view has been advanced and ably advocated by Kirkes, Hughlings Jackson, Broadbent, and others, that it is to endocarditis rather than to pericarditis that we have to look for the explanation of the choreic phenomena. The theory is, that some of the particles of lymph, effused on the surface of the valves, get detached, enter the circulation, and cause embolic plugging of the minute

[1] Begbie, op. cit., p. 84.

vessels of the motor ganglia, and some pathological evidence has been adduced to show that the corpora striata and optic thalami have suffered in fatal cases of chorea. The actual existence of embolism, however, has not been demonstrated, and its occurrence, as a cause of chorea, cannot be regarded as more than hypothetical. That such an event is possible, there can be no doubt; but if particles of fibrine are detached from the valvular surface, it is difficult to see why the vessels of other parts of the brain should not be plugged, as well as those of the motor ganglia, and why these embolic particles should not sometimes get into other organs, and give rise to infarctions of the lung, spleen, kidney, etc.

Again, if the cause of chorea in rheumatic subjects be the detachment of particles of lymph from the surface of a roughened valve, how are we to explain its occurrence in those numerous rheumatic subjects whose valves have never been affected? To such cases this embolic theory is quite inapplicable. It cannot, therefore, be regarded as adequate. Just as Bright's theory might apply to cases of chorea occurring in connection with pericarditis, so this one might apply to cases of chorea occurring in connection with endocarditis. The fault of each is its narrowness, and the impossibility of applying it to more than a minority of the total cases of rheumatic chorea. What we want is an explanation which will apply to all cases of that disease—those occurring in connection with pericarditis—those occurring in connection with endocarditis—those occurring in connection with simple rheumatism of the joints, uncomplicated by any heart affection—and those occurring in persons of rheumatic constitution, but who, at the time of the choreic attack, are not suffering from rheumatism of either the heart or joints.

The theories hitherto advanced have given prominence to two different factors—the morbid condition of the blood, and the inflamed condition of the heart. Neither has been sufficient to meet the whole of the facts. A much wider pathological view is required for that purpose. Such a view we have in the theory advanced in these pages as to the nature of rheumatism.

Rheumatism is essentially a disease of the motor apparatus: chorea is essentially a disease of the motor centres.

In this broad pathological statement we have the clue to the explanation of the relation of the two diseases.

The motor centres affected in chorea, and the motor apparatus which suffers in rheumatism, have an essential physiological connection. The motor centres form the central portion of a system, of which the motor apparatus is the distal or peripheral. Each is essential to the physiological completeness of the other, and without the other, neither has any physiological *raison d'être*. Without joints to be moved the motor centres would be useless: without motor centres to initiate the necessary nervous force, the muscles would remain flaccid, and the joints be of no avail.

The seat of chorea and the seat of rheumatism having so close a physiological connection, it need not surprise us to find that there is some connection between these two diseases, and that those who are subject to the latter, are also liable to have the former.

The existence of the rheumatic diathesis implies a liability to disturbance of the motor apparatus. The motor ganglia are an essential part of this apparatus. Those subject to rheumatism are therefore, *cæteris paribus*, more likely to have susceptible motor centres than those who are not. Thus the rheumatic diathesis predisposes to chorea. So much physiology teaches. But the practical questions still remain—How is the chorea induced? What is its exciting cause? and Why does it occur only in a small percentage of the total number of rheumatic subjects?

Here, as in the case of the nervous symptoms of pericarditis, constitutional predisposition plays an important part. The motor centres, like all other parts of the nervous system, are more susceptible, and more liable to disturbance, in females than in males, and in young people than in those of more mature years. We accordingly find that it is in females and in young people that choreic symptoms are most apt to show themselves. The rheumatic constitution is by no means necessary to their production. A fright, or nervous shock, gastric or uterine derangement, may give rise to chorea and be the exciting cause of the disease in persons in whom there is no history of rheumatism. But many cases there are—so many that the connection is too striking to have escaped detection—in which a present or prior rheumatic attack, with or without heart affection, is the only cause to which the chorea can be traced. Many cases there are, too, in which a rheumatic family history forms the only noteworthy feature.

In discussing the pathology of rheumatic chorea, we thus have two different classes of cases to deal with—those in which the chorea occurs either in connection with, or subsequent to, a rheumatic attack, and those in which there is only a family history of rheumatism.

A rheumatic attack means inflammation of an essential and important part of the motor apparatus, and general disturbance of the whole system. If a nervous shock, or derangement of the digestive or uterine organs, may induce chorea in one predisposed to it, a rheumatic attack may almost certainly do so too, for general rheumatic disturbance of the motor apparatus cannot but be regarded as a possible cause of disturbance of the motor centres. Thus the rheumatic diathesis may be the predisposing, and the rheumatic attack the exciting cause of an attack of chorea. The essential connection of these two causes, and their combination in the same subject, suffice to explain the special tendency of chorea to occur in those who have suffered from rheumatism. The heart complications, to which the choreic phenomena are by some ascribed, are a mere incidental accompaniment of the disease. They may, of course, act as an exciting cause in the same way as the joint affection, but they are not essential to the production of chorea.

But the predisposing cause may exist without the exciting. There may be a family predisposition to rheumatism, without the disease having ever occurred in a given member of the family. With this predisposition there may be combined a special susceptibility of the motor centres, predisposing to chorea; and, for reasons already given, this special susceptibility is more likely to exist in one of rheumatic than in one of non-rheumatic family. Choreic symptoms may show themselves in such a one without any prior rheumatic attack, the exciting cause being some other disturbing agency, possibly one that it may be very difficult to detect, so slight are the causes that may produce disturbance of the nervous centres in young persons predisposed to its occurrence. But no matter what the exciting cause, the disease is fitly described as one of rheumatic chorea, if we recognize that what tended to its production and predisposed to its existence was the rheumatic constitution of the individual.

In a rheumatic subject predisposed to chorea through a susceptible condition of the motor centres, it is an accident whether the chorea,

when it does occur, comes on in connection with a rheumatic attack, subsequently to it, or prior to, and independently of, it. The ultimate pathological explanation of the relation of the rheumatism and the chorea is the same in each; the one disease consists in functional disturbance of the external motor apparatus of the body, the other consists in functional disturbance of its internal motor centres.

CHAPTER XX.

RHEUMATIC HYPERPYREXIA.

In 1867, Dr. Sydney Ringer[1] recorded three cases of rheumatic fever in which, after a week or two of illness, marked only by such symptoms as are common in that disease, there were suddenly developed alarming nervous symptoms; the patients rapidly passed into a state of coma, and speedily died. Coincidently with the onset of these symptoms, there was noted a very remarkable rise in the temperature of the body.

The first case was that of a woman, aged twenty. "She was very delirious during the whole of her illness" (the case was complicated with pericarditis), "and was especially so on the night preceding her death. With the exception of the delirium all her symptoms grew less severe; but she was always very ill. On the morning of the day of her death, she was much worse. She was very restless, and constantly muttered. If her statement could be relied on, she was free from pain. The eyes were bright, and her face flushed, and her breathing much hurried. She continued thus during the day, and at 5 p.m. she was discovered by the nurse to be unconscious. I was sent for at 6.30 p.m., when her breathing was stertorous, and she was profoundly insensible. She died about half an hour after that time. Her temperature was always high. Thus, on the first five days of her stay in hospital it rose to 105°. On the next two days, those immediately preceding her death, it marked only 104°. On the morning of her death, at 9 a.m. it was 105°; at 12, 106.2°; at 3 p.m., 106°; and at, 6, half an hour before her death, 109.2°."

The second case was that of a man, twenty-three years of age, in whom, with the usual symptoms of acute rheumatism, there was evidence of both endo- and peri-cardial mischief, though not to any great extent. "The temperature of his body daily rose to 103.4°, until two days before his death. On the evening before he died it was

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[1] Medical Times and Gazette, Oct. 5, 1867.

105.4°. At 8 a.m. of the day on which he died it was noticed that he wandered, but this was thought by the nurse to be 'temper.' At 8.30 I was sent for; he was then very delirious; he rolled violently about the bed, and required to be held down. This violence quickly passed away, and he then lay in a half-unconscious state, and moaned loudly. His breathing was irregular and jerking. His eyes were wide open: the pupils were equal and of medium size. The unconsciousness soon deepened, and he could not be roused. He became very pale and rather livid. The lidivity soon greatly increased. His heart, while in this state, beat most violently. His pulse was regular in rhythm and force, and beat 186 in the minute. At 8.40 the temperature of his body was found to be 109.4°; it gradually rose, and at 9.15, the time of his death, it was 110.8°."

The third case was that of a woman, twenty-nine years of age, about whose case there was nothing remarkable till the alarming symptoms came on. "At the time of her admission she suffered from pain in most of her joints; she was always free from pain in the head, and was not delirious till the night before her death. The temperature of her body rose daily to 101° and 102°; but on the evening preceding her decease it reached 104.2°. With the exception of this rise of 2°, up to this time she appeared to be in the same state she had been in on previous days. At about 9 p.m. of this evening she was delirious, and talked much during the night. She got out of bed several times. At 5 a.m. of the following morning she was much quieter. On entering the ward at 9 a.m. I noticed she was very ill; she appeared to be very restless, and rolled her head from side to side; she took no notice of circumstances around; she appeared to be rather delirious, and muttered much; she often contracted her brows and distorted her face with various grimaces; any request that was made of her was instantly obeyed; thus she protruded her tongue when told, etc. Her temperature at this time was 107.8°. At 9.55 it had risen to 108°, and her pulse beat 144 in the minute. Her heart throbbed strongly. At this time her face was flushed, and slightly moistened with perspiration. Her lips, which were dry, had on them some sordes. The pupils were equal and of medium size. Her breathing was irregular, now quick, now slow, always superficial. There was no paralysis of any of her limbs. At 11.20 she was much worse; the insensibility deepened until she

became quite unconscious of pain. Her arms then fell heavily; they occasionally twitched; now it was observed her breathing was stertorous, and that her face had become pale and rather livid. Mucus dried on her eyes; her pulse beat 152 in the minute. 11.38, temperature 109.4°; at this time blood was taken from her arm: 11.55, bleeding discontinued; twelve ounces of blood were withdrawn. She was not in any way benefited by the bleeding; her symptoms and temperature continued the same; and at 12.10 the temperature was 110°. At 1.15 her temperature was 110.8°. At this time she died."

Since the publication of these cases similar ones have been recorded by other observers; and hyperpyrexia has come to be looked upon as one of the most alarming complications of acute rheumatism.

The features common to all the cases are the very high temperature, the prominence of the head symptoms, the tendency to a rapidly fatal termination, and the absence of any *post-mortem* lesion sufficient to account for the alarming symptoms and fatal result.

When death in acute rheumatism is preceded by delirium and coma, one naturally looks to the brain or the heart for an explanation of these symptoms and the fatal termination. But in fatal cases of rheumatic hyperpyrexia there has been found in the brain no lesion, and in the heart only such change as is common in rheumatic fever. In Dr. Ringer's first case "the brain, medulla oblongata, and their membranes were quite healthy." In the second, "the brain and its membranes were healthy, not even congested." In the third, "the brain and its membranes were natural in appearance."

The experience of other observers is the same.

A dark fluid condition of the blood, some congestion of the lungs, and a tendency to rapid decomposition, are the only constant *post-mortem* features. There is nothing in any of these to explain either the symptoms noted during life, or the occurrence of death.

Notwithstanding the absence of local lesion, there can be little doubt that the fatal result in rheumatic hyperpyrexia is due to disturbance of an important part of the nervous centres. The alarming symptoms which precede it, are almost entirely referable to the brain; there is no local complication to explain their occurrence; and death is brought about by coma—by failure of cerebral action.

The questions which suggest themselves for our consideration, are

(1) the mode of production of the high temperature, and (2) the relation which this bears to the brain symptoms and the fatal result.

1. *The mode of production of the high temperature.*

The high temperature of rheumatic hyperpyrexia is due to one of two agencies: either it results from an excess of the same cause which gives rise to the increased heat of ordinary cases; or it results from the operation of an agency peculiar to the cases in which it occurs.

Were hyperpyrexia simply an excess of the ordinary pyrexia of acute rheumatism, and produced in the same way as that, it would occur only in cases marked by unusual prominence of all the symptoms, local as well as general. If the pyrexia of ordinary cases result from the propagation of the rheumatic poison in the system, and coincident inflammation of the fibrous textures; and if the degree of pyrexia be directly as the extent of this propagation and inflammation (as it certainly is); then hyperpyrexia, if simply an exaggeration of the ordinary pyrexia, would be symptomatic of an unusual development of the rheumatic poison, and cases in which it occurs would be characterized by inordinate severity of the rheumatic symptoms. But such is not the case. In those in whom hyperpyrexia has been developed, the disease has, up to the time of its occurrence, presented no peculiar feature. The temperature, the joint pains, the acid sweats, the cardiac complications, the condition of the secretions, have all been such as are daily met with in ordinary cases of rheumatic fever. Prior to the occurrence of hyperpyrexia there has been observed, in the history and course of these cases, nothing to distinguish them from ordinary rheumatic attacks, and nothing to lead one to anticipate the occurrence of so alarming a complication.

Clearly rheumatic hyperpyrexia cannot be regarded as simply an excess of the pyrexia of an ordinary rheumatic attack.

It is an exceptional phenomenon, occurring in only a fractional proportion of the total cases of acute rheumatism. An exceptional occurrence is due to an exceptional cause, and calls for an exceptional explanation. The only exceptional agency which offers itself for our consideration, is some peculiarity of the individual in whom the hyperpyrexia occurs. The question of its causation, therefore, narrows itself into a consideration of the possibility of any individual peculiarity giving rise to such a result.

The temperature of the healthy human body is 98.4°. It is kept up by the heat produced during the various changes, assimilative and disintegrative, which are constantly going on in the tissues.

But if heat-production were constantly going on, without anything to counterbalance it, heat would accumulate in the system, and the temperature would rise above 98.4°. The counterbalancing agency is the heat discharge which is constantly taking place from the pulmonary and cuticular surfaces, chiefly the latter.

Heat is a product of tissue change, just as urea and carbolic acid are; and, like them, requires to be eliminated. The maintenance of an unvarying and equable temperature means the establishment of a proper equilibrium between the heat-producing and heat-eliminating processes. In the healthy body the heat produced varies much from time to time; but increased production is counterbalanced by increased elimination, and the temperature does not rise. During muscular exercise, for instance, there is a great increase in those tissue changes during which heat is formed, but there is not a corresponding rise in the temperature of the body; for the exercise which causes this increased production, is accompanied by a counterbalancing increased frequency of respiration, and increased activity of the skin. There is a feeling of increased heat because of the more active circulation through the skin, but the temperature of the blood is that of health. Just as increased formation of urea leads to increased action of the kidneys, so increased formation of heat gives rise to increased action of the skin, and consequent increased discharge of heat.

But it is extremely unlikely that this delicate equilibrium could be so persistently maintained amidst such constantly occurring changes in heat production and discharge as are inseparable from the daily routine of man's existence, and the widely different and ever-varying conditions of life and climate which he is called upon to face,—it is extremely unlikely that this delicate and finely adjusted counterpoise of production and elimination could, under such circumstances, be so constantly maintained, solely by the crude chemical and physical conditions of tissue change and surface transpiration; or that tissue change and heat discharge should, under all healthy circumstances, be so accurately counterbalanced, that the former could never raise the temperature above, and the latter never make it descend below, the standard of

health. The constancy with which, under the most varied conditions of life and climate, this equilibrium is maintained, points to the existence, besides these purely physical agencies, of some central controlling power, on whose ever-vigilant action the maintenance of this finely adjusted balance is dependent; and which presides over and regulates the production and elimination of heat, just as the motor centres preside over the production, regulation, and proper utilization of muscular movement; and just as the vaso-motor centres control and regulate the distribution of the circulating fluid. Without some such regulating centre, it is difficult to see how the temperature equilibrium could fail to be frequently disturbed by agencies which, as it is, have no effect upon it.

The tendency of modern research is more and more towards the recognition of the doctrine of the localization of cerebral action, according to which circumscribed and limited portions of the brain and cord are believed to preside over, control, and regulate particular acts and functions.

Just as there are centres for the special senses of sight, hearing, taste, etc., so do there exist centres for speech, imitation, mastication, deglutition, etc., whose position in the nervous centres can be defined with more or less exactness. We recognize too, and define the position of, a respiratory centre, a cardiac centre, and a vaso-motor centre.

With the localization of cerebral function thus demonstrated in so many cases; and with the position of various controlling centres more or less accurately circumscribed and defined, we have good *a priori* grounds for regarding the existence of a "thermic centre" as at least probable.

And there is not a little evidence, both physiological and pathological, that such a centre does exist.

The tendency of physiology is towards the recognition of a special set of thermal nerves, distinct from the ordinary nerves of sensation, and having for their function the conveyance to the brain of impressions of heat and cold. When, for instance, I touch any part of the surface of my body with a cold brass button, I feel that the button touches me, and that it is cold. If I touch myself again with the same button slightly warmed, I feel that it touches me as before, but that it is no longer cold. Here there are two distinct impressions: first, that made

on the ordinary nerves of sensation, and by which I know that I am touched; and second, that made on the thermal nerves, by which I know that the button is cold or warm.

If I get into a bath at the temperature of 100°, I feel the water touch me, and know that it is a liquid; but I feel also that it is warmer than a bath of 98° which I may have just got out of, and not so warm as one of 102° into which I may get afterwards. Here there is the same double sensation—that of touch, and that of temperature.

These two sensations are distinct and separate; and one may be felt without the other. I touch the skin of my face with the feathery end of the quill with which I am writing. I feel the touch; but there is no sensation of heat or cold. The nerves of sensation receive the impression: the thermal are not affected by it. I go into a cold room, I allow the fire to go out in that in which I am writing, or I put on thinner clothes than usual, and I feel the change of temperature. I can tell at once whether the temperature of a room is high or low; whether my feet are cold or warm. This knowledge I get through impressions conveyed by the thermal nerves, and without any aid from the nerves of sensation.[1]

Other evidence in favor of the recognition of special thermal nerves we have in the fact that some parts of the body are more susceptible than others to temperature impressions, without being more susceptible to ordinary touch impressions. If, for instance, I wish to test the heat of a poultice, I do so with the back of the hand rather than with the palm, because I know from experience that the back receives thermal impressions more readily than the palm. But to ordinary touch sensations the palm is more susceptible than the back.

There are other reasons for regarding the existence of special thermal nerves as, at least, not improbable. It is extremely unlikely that the same nerve should be able, at one and the same time, to convey two distinct impressions, or that the same portion of the nervous centres should be capable of simultaneously registering them. The simultaneous conveyance to the brain of two such entirely distinct impressions as those which we have been considering, points to their conveyance by

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[1] Brown-Séquard thinks there are four different special conductors for (1) touch, (2) tickling, (3) temperature, and (4) pain.

two distinct sets of nerves. The existence of two distinct sets of nerves almost necessarily presupposes two distinct centres—one for each—in which the special impressions of each set of nerves are registered. A belief in the existence of thermal nerves almost necessarily carries with it a belief in the existence of a thermic centre.

That physiology affords reasonable grounds for such a belief, we have just seen.

Pathology, too, points in the same direction.

1. It has been shown by direct experiment that section of the pons at its junction with the medulla oblongata, causes the temperature of an animal to rise.

2. Injuries and diseases of the nervous centres and their membranes, and especially of the cervical portion of the cord, are often accompanied by a very remarkable rise of temperature, for which there exists no reason except the nervous lesion. Since Sir Benjamin Brodie[1] recorded his well-known case, similar ones have been observed by others, in which, after injury to the cervical cord, the temperature of the body rose to 109°, 110°, or 111°. And Mr. Teale[2] has related one in which a patient recovered after the temperature had reached the unprecedented height of 122°.

But in some cases of injury to the cervical cord, the opposite condition is noted; instead of a great rise, there is a great fall of temperature. Mr. Hutchinson[3] has related an instance of crushing of the cord at the level of the fifth cervical vertebra, in which, within twenty-four hour after the injury, the temperature in the urethra was 93°, and in the rectum 95.8°.

3. Pathological records, too, show that when the nervous supply to a given part is arrested by injury or disease, the temperature of the part thus isolated falls below the normal. This fact has been attributed to diminished functional activity of the paralyzed part, and consequent decreased blood supply. But that explanation cannot apply to all cases. "When, for instance, after section of the ulnar nerve, the temperature

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[1] Medico-Chirurgical Transactions, 1837.

[2] Transactions of Clinical Society of London, 1875.

[3] Clinical Lecture on the Temperature and Circulation after Crushing of the Cervical Spinal Cord, by Jonathan Hutchinson, Senior Surgeon to the London Hospital. (*Lancet*, May 22, 1875.)

at a late stage becomes so much altered that several degrees of loss are registered when the thermometer is put in the cleft between the little and ring fingers of the injured hand, we are quite unable to call in to our aid any theories of altered blood supply. The vaso-motor is uninjured, and the arteries supplying the cooled part are branches of the same trunk which feeds others which remain warm." [1]

It has been suggested that the profound modifications of temperature caused by injuries of the cervical cord, are really due to altered conditions of the circulation, consequent on injury of the vaso-motor centres; and that paralysis of the inhibitory function of that centre, by causing increased fulness of the cutaneous vessels, leads to increased elimination of heat, and consequent lowering of the temperature of the whole body. In the more numerous cases in which there is the opposite condition—a great rise of temperature—the result is attributed to increased activity of the heat-producing processes.

But to say that there is increased activity of the processes by which heat is produced, is to indicate, not to explain, the rise of temperature. What we want to know is why, in such injuries, these processes are more active, and why this increased activity on their part is not counterbalanced by a corresponding increase in heat discharge.

It is quite evident that no altered condition of the circulation, and not even the most extensive and violent inflammation, could, in a few hours, raise the temperature twelve or thirteen degrees above the normal standard; it is equally certain that no amount of ordinary tissue change could produce such a result.

There is no reason why, in injuries of the cervical cord, tissue change should be more active; and there is no evidence of its being so.

Neither is there any apparent reason why, in such injuries, the ordinary heat-eliminating action of the cutaneous surface should cease, and heat accumulate in the system; for the physical condition and relation of the skin and of its environment are unchanged.

In short, it is impossible to explain the great alteration of temperature, resulting from injury to the cervical cord, by a reference to any of the ordinary physical causes of heat production and elimination.

The conclusion is forced upon us, that the great rise of temperature

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[1] Hutchinson, loc. cit.

which accompanies such injuries, is essentially associated with the *seat* of the injury, and not with its nature or extent; for similar injuries in other parts of the cord produce no such effect.

To regard injury of a limited portion of the nervous centres as being *per se* a cause of a great rise of temperature (as we unquestionably do regard injury of the cervical cord), is to invest the injured portion with a heat-modifying power, which is quite above, and distinct from, the results of tissue change and surface transpiration. It is, in short, to recognize the existence in it of a special thermic centre.

Such a centre can have but one function—to control and regulate the production and elimination of heat.

The blood plays such an important part as a distributing agent, that the centre which controls heat distribution is likely to have some working relation with that which controls the distribution of the circulating fluid. The vaso-moto centre and the thermic centre are, therefore, likely to have their seat in the same part of the nervous system. The former, we know from the experience of Ludwig, Schiff, etc., has its seat in the cerebral and spinal medulla. The latter, there is reason to believe, has its seat in or about the same locality.

Seated in the same part of the nervous system it is all but inevitable that injury of that part should cause disturbance both of the vaso-motor and thermic centres—the former evidenced by marked changes in the circulation, the latter by marked change of temperature.

The great change of temperature noted in injury of the cervical cord, has no essential connection with, or causal relation to, the altered condition of the circulation, which is sometimes associated with it. Both are to be regarded as conjoint results of injury to the upper part of the cord—the seat of both the vaso-motor and thermic centres.

Our position, then, is as follows:—

We believe (1) that there is a special thermic centre, seated probably high up in the cord, controlling and regulating the temperature of the body; (2) that this centre is endowed with heat-producing and heat-inhibiting powers; (3) that it has intimate physiological and anatomical relations with other important centres; (4) that it has connected with it a special set of thermal nerves, distinct from the ordinary nerves of sensation; (5) that these nerves are very freely distributed to the skin.

The thermal apparatus thus consists of a central, and a peripheral portion. Each is essential to the functional completeness of the other. Impressions pass from the central to the peripheral, and from the peripheral to the central.

How profoundly the temperature of the body may be altered by central lesions, is evidenced by what is noted in connection with injuries of the cervical cord.

What we have now to do, is to explain the occurrence of a similar change independently of such a lesion.

Besides central lesions, peripheral impressions form the only means by which disturbance of the thermal apparatus could be produced.

It is quite possible that such impressions — that is, impressions originating on the cutaneous extremities of the thermal nerves, and transmitted thence to the thermic centre—might be sufficiently powerful and prolonged to produce serious disturbance there, and even cause such rise of temperature as is noted in connection with central lesions.

The question before us thus narrows itself into a consideration of the point as to whether or not, in the diseases in connection with which hyperpyrexia occurs independently of central lesion, there exists any cause of peripheral disturbance, competent to produce such a result.

The only two morbid conditions in connection with which such hyperpyrexia is habitually found to occur, are heat-stroke and acute rheumatism.

The question thus further narrows itself into a consideration of the point as to whether or not, in heat-stroke and acute rheumatism, there exists any cause of serious disturbance of the thermal peripheræ.

It is evident that in both of these there may be considerable disturbance of the cutaneous thermal peripheræ; for in the one there is always exposure of the surface of the body to a high temperature, and the other has for one of its prominent characteristics, unsually free action of the skin.

The hyperpyrexia of acute rheumatism cannot be rightly considered without reference to the same condition as it presents itself in heat-stroke. The conjoint consideration of these two morbid conditions cannot fail to force on our attention their strong resemblance to each other. The morbid condition which most resembles rheumatic hyperpyrexia, is heat-stroke; the morbid condition which most resembles

heat-stroke, is rheumatic hyperpyrexia. In both, the prominent symptoms during life, are great rise of temperature, alarming nervous symptoms, and a tendency to a speedily fatal termination. In both, the only constant *post-mortem* features, are a tendency to rapid decomposition of the body, a fluid condition of the blood, and more or less congestion of the lungs. Indeed, apart from differences in their history —involving in the one case, exposure to a high temperature, and in the other the prior occurrence of rheumatic symptoms—the description of the one might almost apply to the other.

The circumstances which lead to the occurrence of the hyperpyrexia of heat-stroke, being so much more apparent than those which lead to the onset of the same symptom in acute rheumatism, a brief consideration of its mode of production in the former, may usefully precede our inquiry into its causation in the latter.

Heat-stroke is produced in one of two ways: either by the direct action of the sun's rays on the head and upper part of the spine; or by a more prolonged exposure of the whole body to a high temperature, with or without any direct action of the sun. The former is a veritable sun-stroke—a true *coup de soleil;* the latter a heat-stroke, properly so-called.

In considering the pathology and mode of production of heat-stroke, allowance must be made for these two different forms of heat action. For though the morbid state to which each gives rise may be practically the same, there is a considerable difference in its mode of production in the two cases.

In *coup de soleil,* due to direct exposure to the sun's rays, the patient is struck down without previous warning, and the seizure is rightly attributed to the direct action of the sun's rays on the head and neck. That it is thus produced, is evidenced by the fact that the accident may be guarded against by proper protection of these parts.

Sunstroke, thus induced, varies in severity. The seizure may be so violent as to prove almost immediately fatal; or recovery may be more or less complete. The symptoms vary with the severity of the stroke, and with the extent of the nervous lesion. If the cerebrum is mainly affected, the symptoms will be chiefly those of cerebral disturbance; if

the upper part of the spine suffer, the functions of organic life will be interfered with and the danger to life be correspondingly great.

The thermic centre, we have seen reason to believe, has its seat in the cervical cord. In the history of sun-stroke, there is no fact better established than that protection of the back of the neck is as important as protection of the head; and all the coverings and head-pieces used by Europeans resident in tropical climates are so constructed as to afford this double protection: it being universally recognized that exposure of the back of the neck is as hazardous as exposure of the head.

The hyperpyrexia which occurs in cases of sun-stroke thus induced, is due to the direct action of the sun's rays on the insufficiently protected thermic and other centres; and is, both etiologically and pathologically, more allied to that which occurs in connection with lesions of the cord, than to that which occurs in connection with acute rheumatism.

It is otherwise with the more slowly induced heat-stroke, due to prolonged exposure of the whole body to a high temperature. Here there is no special exposure of the head or neck; and the seizure may come on during the night as well as during the day. It is more apt to occur when, with exposure to heat, there is combined exhaustion from fatiguing exercise—as in soldiers after a long march. Its occurrence, too, is favored by anything which interferes with the free play of the lungs, such as tight or unsuitable clothing; or by anything which prevents these organs from performing their function aright, such as breathing a vitiated atmosphere.

Such are the facts. How are they to be interpreted?

That prolonged exposure to a high temperature is likely, in a native of a temperate climate unaccustomed to such exposure, to cause some disturbance of the thermal apparatus, there can be no doubt. Heat is a normal product of tissue change, ranking in this respect with urea and carbonic acid, and, like them, requiring to be eliminated. Its chief channel of elimination is the skin. Anything which interferes with this heat-eliminating function, may lead to the retention of heat in the system. And thus the atmosphere of a tropical climate might act. For just as an excess of carbonic acid in the atmosphere is a bar to the elimination of that gas from the system, so the presence in the atmosphere of an undue amount of heat is a physical obstacle to

the ready elimination from the body of the heat formed therein. Thus, prolonged exposure to a high temperature might lead to the retention of heat in the system, and mere residence in a tropical climate be a cause of disturbance of the thermic centre.

But there is a safeguard against this; for the same cause which makes the elimination of heat more difficult, produces also increased action of the skin: and this latter effect is a counterbalancing agency to the former. The possibly injurious effects of such prolonged exposure to heat as is inseparable from residence in a hot climate, are thus met by increased activity of the heat-eliminating surface.

It is evident, however, that under such circumstances the due quantity of heat can be eliminated only by increased effort of the eliminating apparatus; and that the inhibitory function of the thermic centre must be very actively stimulated. The stimulation must indeed at times amount almost to irritation, so great are the obstacles to the efficient performance of its function. Such irritation might be so great as to cause considerable disturbance of the thermic centre, and so tax its heat-inhibiting power as to render it incapable of responding to any increased call—such, for instance, as that which would result from vigorous or prolonged muscular exercise; or that which would follow interference with the action of the lungs—the other channel of heat elimination.

It is probable that this is what really occurs in cases of heat-stroke. There is considerable and constant irritation of the peripheral portion of the thermal apparatus—an irritation which must be transmitted to the central portion, producing there an amount of disturbance which may not suffice to cause disorder, but which may be enough to tax to the utmost its heat-inhibiting power, and render it incapable of responding to any increased call. Under such circumstances, increased exposure to heat, as to the sun's rays; a few hours' exercise; or a night spent in a badly ventilated room, might upset the already tottering balance, and produce more or less complete paralysis of the heat-inhibiting centre. The heat-producing portion of the thermic centre being thus left in uncontrolled possession of the field, the temperature would speedily run up, and hyperpyrexia result.

There is no difficulty in understanding how heat might produce such a result, if we only regard it as an excretory product, requiring to

be eliminated. Just as excess of carbonic acid in the blood stimulates the respiratory centre, and leads to increased force and frequency of respiration—so an excess of heat stimulates the thermic centre, and leads to increased activity of the heat-eliminating process.

If stimulation of the respiratory centre be carried beyond a certain point, it results in paralysis; respiration gradually ceases, and the animal dies asphyxiated. So it is with the thermic centre—if its stimulation be carried beyond a certain point, it may result in paralysis of its heat inhibiting or eliminating function, and consequent hyperpyrexia.

That heat elimination is diminished in heat-stroke before the onset of alarming symptoms, is evidenced by the fact noted by Morehead[1] and others, that the seizure is apt to be preceded for some days, not only by headache, giddiness, and other evidence of disturbance of the nervous centres; but by a dry and unperspiring condition of the skin—a condition which clearly points to serious interference with its eliminating function.

The essential difference between sun-stroke due to the direct action of the sun's rays, and heat-stroke resulting from exposure to a high temperature, is that the former results from the direct action of the sun's rays on the thermic centre; while in the latter, that centre is acted on only indirectly through a more prolonged disturbance transmitted to it from its peripheral portion. It is with the latter that the hyperpyrexia of acute rheumatism has analogies.

But, it may be said, if the action (direct or indirect) of heat on the thermic centre be the cause of the disturbance, why is it that only the inhibitory portion of that centre is affected, and that the heat-producing part is not also paralyzed? The answer is simple. Production is a higher function than elimination, and requires for its performance greater power and more vigor. The part of the thermic centre which presides over heat-production is, therefore, likely to be possessed of a more robust vitality than that which controls inhibition; and especially is this likely to be the case in a native of a temperate climate, in which the habitually low temperature of the atmosphere not only calls for vigorous heat production, but also greatly favors and facilitates heat elimination. Being possessed of less vitality, the heat-inhibiting

[1] Morehead, Clinical Researches on Diseases in India, 1856.

portion may be seriously affected by an agency which has little or no effect on the heat-producing.

When the function of the whole thermic centre is in abeyance, as in severe crushing of the cord, heat production and heat elimination are both put a stop to. So far as its relation to its environment is concerned, the body is, under such circumstances, in nearly the same position as if life had ceased. Its temperature tends to become that of the surrounding atmosphere; and is prevented from doing so only by the continuance of those tissue changes which go on while life lasts. In other words, the temperature falls, as in Mr. Hutchinson's case already referred to.

One of the prominent results of our inquiry into the pathology of heat-stroke, is the inference that disturbance of the thermic centre, sufficient to cause more or less complete paralysis of its inhibitory function, and consequent great rise of temperature, may be produced by irritation of the peripheral extremities of the thermal nerves. In the case of heat-stroke, the irritant cause is prolonged exposure to a high temperature under unfavorable circumstances.

If any other agency were capable of giving rise to similar irritation of the cutaneous surface, it might lead to a like result. And our inquiry into the causation of the hyperpyrexia of acute rheumatism, involves the consideration of the question as to whether or not there is at work in that disease any cause competent to produce such disturbance of the thermal peripheræ as might upset the thermic centre.

One of the prominent features of an attack of acute rheumatism is excessive action of the skin—the same result which habitually follows prolonged exposure to a high temperature. The cause of the profuse perspirations of acute rheumatism, is the presence in the blood of an excess of lactic acid. This acid has, on the cutaneous surface, even a more decidedly stimulant action than a hot atmosphere. Except heat-stroke, acute rheumatism is the only disease in which such excessive stimulation of the cutaneous surface is constant and habitual: except heat-stroke, it is also the only one in which hyperpyrexia is habitual. If we regard the hyperpyrexia of heat-stroke as an indirect result of excessive stimulation of the cutaneous surface, we can scarcely avoid the inference that the hyperpyrexia of acute rheumatism may be simi-

larly associated with the excessive action of the skin, characteristic of that disease—that lactic acid may cause in acute rheumatism, not only the same disturbance of the cutaneous surface which results from exposure to the atmosphere of a tropical climate, but may also indirectly produce a like disturbance of the thermic centre. Certain it is, that if excessive and prolonged irritation of the whole cutaneous surface, and its contained thermal peripheræ, may cause disturbance of the thermic centre, we have at work in acute rheumatism an agency competent to produce such a result.

The disturbing effect of lactic acid is exercised primarily on the water-eliminating function of the skin—that of a tropical atmosphere on the heat-eliminating; but the two functions are so inseparably associated, that stimulation of the one necessarily involves stimulation of the other. Thus we have at work in acute rheumatism an agency similar to that which operates in heat-stroke, and to whose indirect action we believe the hyperpyrexia of this latter to be attributable: and thus the inference is presented to us, that the hyperpyrexia of acute rheumatism, like that of heat-stroke, may be due to disturbance of the thermic centre, consequent on irritation of the thermal peripheræ.

2. *The relation of the high temperature to the brain symptoms, and the fatal result.*

There are two views on this point. According to one, the high temperature is primary, and the nervous symptoms secondary; according to the other, the nervous disturbance is primary, and the high temperature secondary.

According to the former, which has been advocated by Liebermeister[1] and others, the high temperature causes disturbance, and ultimately paralysis, of the nervous centres. The chief evidence in support of this view, is the frequent association of nervous symptoms with an unusually high temperature.

In acute rheumatism a very high temperature is always accompanied by such symptoms; but it is not so in all diseases. Reference has already been made to a case recorded by Mr. Teale in which a temperature of 122° produced no serious disturbance. The case is so unique, that one does not care to do more than merely refer to it. But in re-

[1] Deutsch. Arch. für Klin. Med., Vol. I., 1866.

lapsing fever it is not uncommon to find the body heat run up to 106°, 107°, and 108°, without giving rise to any disturbance of the nervous centres. "High temperatures in relapsing fever entail little or no danger to the patient, and do not produce serious nervous symptoms. Of Obermeier's patients the temperature of three rose to 107.6°, of six to 107.7°, and of two to 108.5°. In all these cases no special danger attributable to the high temperature could be discovered, nor even a single circumstance in which they differed from the rest." "During the attacks," says Tennent, "the height attained by the temperature was on an average between 104° and 106°. In many cases, however, it was found to be as high as 107°, while in two cases 108° was noted. In these cases of very high temperature, the condition otherwise was not in any way notably different."

Of all the continued fevers, relapsing fever is the one in which the body heat has the highest range, and in which the temperature of hyperpyrexia is most frequently noted. Did a high temperature of the blood have, on the nervous centres, the disturbing influence that Liebermeister and others believe it to have, head symptoms would be a prominent feature in relapsing fever. But the reverse is the case; for they are much less marked and frequent in it than in typhus and typhoid fevers, in which the body heat is, as a rule, less elevated.[2]

In acute rheumatism a temperature of 107° or 108° is always accompanied by alarming nervous symptoms; but with such an absolute demonstration as that afforded by the case of relapsing fever, that this rise may cause no unusual symptoms, it is impossible to accept the view that in rheumatic hyperpyrexia the high temperature is the cause of the nervous disturbance.

There is ample evidence to show that lesions of certain parts of the nervous centres may cause an unusual rise of temperature. There is not sufficient evidence to show that unusual elevation of the body heat may cause disturbance of the nervous centres.

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[1] Murchison, On the Continued Fevers of Great Britain, 2nd ed., p. 356.

[2] A temperature of 106° to 108° occurring in relapsing fever is an ordinary feature of the disease. It is produced by the propagation of the contagium in the blood, in the same way as the ordinary pyrexia of acute rheumatism. For a detailed account of the mode of production of the pyrexia of the continued fevers, the reader is referred to the author's work on The Germ Theory of Disease, already referred to.

In rheumatic hyperpyrexia there are both high temperature, and serious nervous symptoms: in relapsing fever there is only high temperature. It is evident that the state of matters with which we have to deal in rheumatic hyperpyrexia, resembles that which presents itself in relapsing fever with high temperature, less than it does that noted in lesions of the upper part of the cord, and in these there can be no doubt that the high temperature is secondary to the central lesion.

Moreover, it is incumbent upon us to explain the occurrence of the high temperature. But, on the view that it is primary, how are we to do so? In the absence of prior disturbance of the nervous centres, what possible reason is there for the rise? Absolutely none. And surely no view of the mode of production of the general condition to which we apply the term hyperpyrexia, can be accepted as adequate, which does not even attempt to explain one of its most prominent and characteristic features.

Those who regard the high temperature as the cause of the nervous symptoms of rheumatic hyperpyrexia, have committed the same fatal error that was made by the advocates of the lactic acid theory—they have taken one of the symptoms of this condition, and have raised it from its subordinate position of a symptom, to the rank and dignity of an exciting cause.

It is evident that the view that the nervous symptoms of rheumatic hyperpyrexia are caused by the high temperature, lacks the support which would commend it to our reason.

The alternative view, that the high temperature is secondary to disturbance of the nervous centres, more readily commends itself to us. There is not only no distinct evidence that a high temperature of the body ever causes disturbance of the nervous centres: but there is distinct evidence, first that such temperature frequently occurs without any such result; and second, that disturbance of the nervous centres may cause unusual rise of temperature.

If we acknowledge the existence of a connection between the high temperature and the nervous symptoms of rheumatic hyperpyrexia, we must, in the light of such evidence, accept the view that the high temperature, and the alarming symptoms which accompany it, are associated together, not as cause and effect, but as conjoint results of some disturbing influence acting on the nervous centres.

It has already been shown how disturbance of the thermic centre, and consequent great rise of temperature, might be indirectly brought about in acute rheumatism by the irritant action of lactic acid on the thermal peripheræ.

If the thermic centre be situate, as we believe it to be, in or about the spinal medulla, it is situate in a part of the nervous system which is also the controlling centre of the most important functions of organic life. Any serious interference with the functional integrity of these centres, must be accompanied by alarming symptoms, and danger to life. Thus it is that a high temperature in acute rheumatism is accompanied by such alarming symptoms, and so great danger. Situated as it is, at the upper part of the cord, and intimately associated as it is, both anatomically and physiologically, with other important centres, the thermic centre cannot be seriously disturbed without there being produced also some disturbance of the vaso-motor, nutritive, cardiac, and respiratory centres, situate in its immediate neighborhood, and possibly in direct contact with it. The greater the disturbance of the thermic centre, the greater would be, not only the rise of temperature, but the participation of contiguous centres in that disturbance. Hence the greater the rise of temperature, the greater the danger to life—not because the high temperature is in itself a danger, but because what induces that symptom causes also other and more serious ones. The prominence of all the effects is directly as the extent of the causal disturbance.

The results of *post-mortem* examinations of fatal cases of rheumatic hyperpyrexia, are in keeping with this view of its mode of production. Functional disturbance of such important centres as those involved, might cause a fatal result, without leaving behind any lesion recognizable after death, and thus might be explained the negative results of examination of the nervous centres. The congestion of the lungs, which is so commonly noted, might, and probably does, result from disturbance of the vaso-motor, respiratory, and cardiac centres. The fluid condition of the blood points to disturbance of the nutritive centres. While the only other constant *post-mortem* feature, unusually rapid decomposition, is attributable to the high temperature of the body at the time of death and for some hours afterwards. Decomposition is more rapid in the body of a man dead of rheumatic hyperpyrexia,

than in one dead of an ailment involving no excessive body heat, for the same reason that it is more rapid in a hot than in a cold climate. Heat promotes such decomposition.

The relation which rheumatism bears to hyperpyrexia, is very like that which it bears to chorea. When considering this latter point we saw (1) that rheumatism was essentially a disease of the motor peripheræ, and chorea essentially a disease of the motor centres; (2) that the motor apparatus affected in rheumatism has an essential and intimate functional connection with the motor centres; and (3) that those whose motor peripheræ were liable to rheumatic disturbance, were more likely to suffer occasionally from disturbance of the motor apparatus, than those in whom no such liability existed.

After the joint affection, one of the most characteristic features of acute rheumatism is the free action of the skin. This involves, as we have seen, possible disturbance of the thermal peripheræ. Now, just as a rheumatic subject is more liable than a non-rheumatic to have his motor centres disturbed, and the symptoms of chorea result—so also is he more likely to have his thermic centre disturbed, and the symptoms of hyperpyrexia result: disturbance of the thermal peripheræ predisposing him to hyperpyrexia, just as disturbance of the motor peripheræ predisposes him to chorea.

But the question naturally arises—if the hyperpyrexia of acute rheumatism be due to disturbance of the thermic and neighboring centres, and if this disturbance be an indirect result of the action of lactic acid on the extremities of the thermal nerves, why is it that it occurs in only a small percentage of cases of acute rheumatism? The stimulant effect of lactic acid is got in every case of that disease; in every case, therefore, it may be said, there ought to be hyperpyrexia, if its mode of production were such as we suppose.

This objection is the same as that with which we had to deal when explaining the head symptoms of pericarditis, and the relation of rheumatism and chorea. These, we saw reason to believe, were to be accounted for, not by any peculiarity of the rheumatic attack, but by some peculiarity of the individual in whom it occurs.

The same explanation is applicable to rheumatic hyperpyrexia. Prior to the occurrence of the hyperpyrexia, there is nothing in the

case to induce one to expect it; or to distinguish the attack from the dozens of similar ones in which no such disturbance takes place. Failing any peculiarity of the case to account for the exceptional symptoms, we can only refer them to some peculiarity of the affected individual. Indeed, an exceptional symptom, especially when that symptom is of nervous origin, is generally due to some peculiarity of the patient.

Just as it is only in a minority of people that the sensorium is so susceptible as to have its balance upset by the onset of pericarditis, and the motor centres sufficiently susceptible for the production of chorea —so it is only in a small percentage of rheumatic subjects that the thermic centre is so susceptible as to be disturbed, and have its balance upset, by such irritation of the thermal peripheræ as occurs in acute rheumatism.

That the thermic centre may be profoundly affected by influences applied to the thermal peripheræ, and that the hyperpyrexia of heat-stroke, and of acute rheumatism, are thus induced, is further evidenced by the results of the treatment of that condition.

It has been abundantly shown in the case of the hyperpyrexia of heat-stroke, that the treatment which affords the best chance of recovery, consists in applying cold to the extremities of the thermal nerves.

"The principle of management is to reduce as quickly as possible the blood heat. This is best effected by rubbing the body over with ice."[1]

It has been shown, too, first and chiefly by Dr. Wilson Fox,[2] that the hyperpyrexia of acute rheumatism calls for the same treatment; and that the immersion of the body in cold water, or the application of ice to its surface, serves not only to reduce the temperature, but to allay, and ultimately get rid of, those alarming symptoms which are associated with it, and threaten a speedily fatal termination.

The view that has been advanced as to the mode of production of the high temperature in rheumatic hyperpyrexia, and of the alarming symptoms which accompany it, affords a rational foundation for this treatment, and an explanation of its success.

If disturbance of the thermic centre be the cause of the hyperpyrexia; and if this disturbance be, in its turn, induced by irritation of

[1] Aitkens, Practice of Medicine. [2] Treatment of Hyperpyrexia.

the peripheral extremities of the thermal nerves, it is evident that the symptoms thus induced are likely to be best met by the application to the same nerves of an agency having on them an action the reverse of that which caused the disturbance. To allay the disturbance of the thermal apparatus is the object in view. Cold is the means best calculated to attain this end. We know what a quieting influence this agency exercises on the nervous system, and that its prolonged application may even cause alarming depression. Its calming and depressing influence on the nervous centres is evidenced by what is observed in those who are long exposed in a very cold atmosphere. A marked tendency to sleep is one of the early indications of danger. So powerful is this tendency, that it can with difficulty be resisted even by those who are aware that, if they once give way to it, the sleep will deepen into fatal coma.

The beneficial action of cold in hyperpyrexia is generally supposed to be a direct result of the lowering of the temperature of the body. But to suppose that the mere lowering of the body heat is sufficient to allay the alarming symptoms, is equivalent to saying that these symptoms are a result of the high temperature; and *that*, we have already seen, is a position which cannot be maintained.

A more probable explanation of the good effects of cold I believe to be, that it acts directly on the extremities of the thermal nerves; and that the quieting influence there produced is transmitted along these nerves to the thermic centre. If kept up for a sufficient time, this influence, like the prior irritation, is communicated to the neighboring centres. And thus, as a consequence of the direct action of cold on the peripheral extremity of the thermal apparatus, there is produced, either by stimulation of the inhibitory, or paralysis of the producing, portion of the thermic centre, a restoration of the balance of these two antagonistic agencies, and an amelioration of all the symptoms which resulted from its disturbance.

Cold seems to allay the alarming symptoms by lowering the body heat, just as the high temperature seemed to induce them. But just as the elevation of the temperature was secondary to, and consequent on, the disturbance of the nervous centres; so it is probable that its restoration to the normal under the influence of cold, is chiefly attributable to the quieting influence of that agency on the disturbed thermic

centre. A certain amount of heat, of course, passes off from the surface; but the cold which passes in (if I may so express it) is the real curative agency. By the cold which passes in, I mean the influence transmitted from the cold surface along the thermal nerves to the thermic centre.

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